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CONDUCTION SYSTEM IN HUMAN HEARTS WITH INTERVENTRICULAR SEPTAL DEFECTS

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IMPROVED techniques in cardiac catheterization and angiocardiography have resulted not only in early diagnosis of cardiac anomalies, but have provided accurate information as to the location, size, and number of developmental defects.[1, 2] The rapid advances in thoracic and open cardiac surgery have kept pace with the above improved diagnostic methods, so that attention has now been focused upon the need for more detailed knowledge of heart anatomy in certain cardiac anomalies.

Defects of the interventricular septum were of particular interest to the authors, for such defects are not an uncommon anomaly and have been closed surgically with success by several investigators.[3-6] The gross anatomy of such human septal defects was described by Lev[7] and classified clinically by Warden[8] and Becu[9] and their co-workers, yet little information was to be found on the intracardiac location of the specialized conducting tissue in hearts with such interventricular septal defects.[10] The need for such a microscopic study was further emphasized recently by Lillehei in the discussion of another paper,[6] when he stated, "the incidence of complete heart block has been about 12 per cent in the patients having ventricular septal defects repaired."

It should be pointed out that the development and microscopic structure of such specialized cardiac elements in the human heart have been studied.[11-14] The excellent histologic studies of Yater and co-workers[15, 16] were unique in that they studied in detail the conduction tissue of 9 human hearts to determine the pathogenesis of bundle branch block, but none of these hearts had septal defects.

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The present study was an attempt to provide more precise anatomic information on the location and course of the specialized conduction tissues of human hearts that had high interventricular septal defects.

MATERIALS AND METHODS

Fifteen human hearts with high interventricular defects were used in this study. All of the specimens had additional cardiac anomalies although no hearts in our series demonstrated any abnormal ante-mortem cardiac rhythm. There were 8 male and 7 female specimens; 14 were from patients 2 days to 3 years of age, while one was from a 27-year-old patient.

The gross specimens were photographed for future reference. The anterior wall of each was cut and marked with India ink for ease of orientation prior to tissue fixation and embedding. Nine were embedded in celloidin, one in paraffin, and 5 specimens were used for gross study under a dissecting microscope (see Figs. 15-18). The 10 specimens used for microscopic study were cut in serial section and stained individually by a Masson trichrome-light-green method. A wax model reconstruction was made of a 2-month-old specimen to demonstrate the position and relationships of the specialized conduction tissues to the septal defect (see Fig. 7).

RESULTS

The specialized tissues of the conduction system were easily identified in sections stained with the Masson technique by their pale stained appearance. All muscular elements were red in contrast to the light-green appearance of the connective tissue elements.

We were surprised to observe extensive hemorrhage in the specialized tissue of 6 of our specimens. Hemorrhage was noted within the A-V node and common bundle of 3 hearts, in only the common bundle of 2 specimens, and within the A-V node of another.

In all 10 specimens, we were able to trace the continuity of the specialized muscle fibers of the conduction system from the atrioventricular node to the common bundle with its left and right bundle branches. As the common bundle (of His, or crus) was followed distal to the fibrous ring, it was located in the posterior margin of the interventricular septal defect in all but 3 specimens. The location and mode of branching of the common bundle is best presented by a description of this structure in the individual specimens.

Specimen 1. (No. A 14-55, white female, aged 2 days.)

As shown in Figs. 1 and 2 this specimen had a thin translucent interatrial septum and patent foramen ovale, as well as a high interventricular septal defect. The location and course of the common bundle and its branches were inserted on the photographs following a study of the serial sections.

Note the position of the common bundle as it proceeded distally in the thin posterior margin of the defect to divide into left and right bundle branches at the top of the interventricular septum (i.e., at the postero-inferior margin of the defect). At the point of origin of the 2 bundle branches, many fascicles of pale stained fibers could be traced from the common bundle and its 2 branches into the more heavily stained muscle fibers of the interventricular septum (the paraspecific fibers of Mahaim[17]).

The large thin left bundle branch and its rami are illustrated in Fig. 2. It should be noted that a small slender fascicle of the left bundle branch coursed under and then ascended anterior to the defect. The main portion of the left branch continued toward the apex of the left ventricle and gave off numerous stout fascicles to the septum, as well as the anterior and posterior walls of the left ventricle.

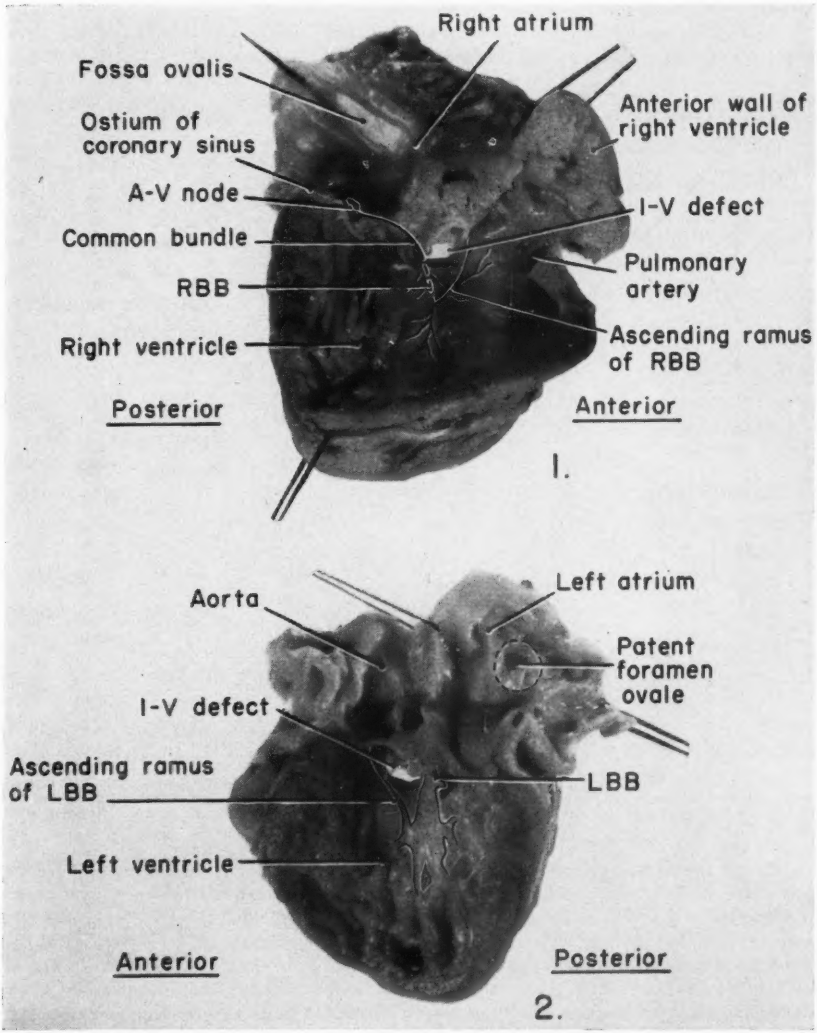

Fig. 1.—Interior of right atrium and right ventricle of Specimen 1. Note relation of the common bundle of conduction tissue to defect within interventricular septum. The right bundle branch (*RBB*) descended in the septal myocardium (dotted) and divided into ascending and descending rami as it reached the endocardium inferior to the defect. The anterior and posterior surfaces of the heart are indicated in this, and all of the following illustrations.

Fig. 2.—Interior of left atrium and left ventricle of Specimen 1. The location of the thin broad left bundle branch (*LBB*) is shown as it descended in the posterior margin of the septal defect. Note ascending ramus of left bundle branch.

The slender right bundle branch descended within the interventricular septum to gain a subendocardial position part way down the right side of the septum as shown in Fig. 1. The right bundle branch also had a small but discrete fascicle of specialized fibers that ascended anterior to the septal defect (Fig. 1). Smaller twigs from the ascending ramus became lost in the myocardium of the septum anterior to the defect.

Specimen 2. (No. A 5774, white female, age 2 months.)

This specimen with a high septal defect (Fig. 3) was one of our most interesting cases, for the specialized elements of the conduction system were extremely well differentiated.

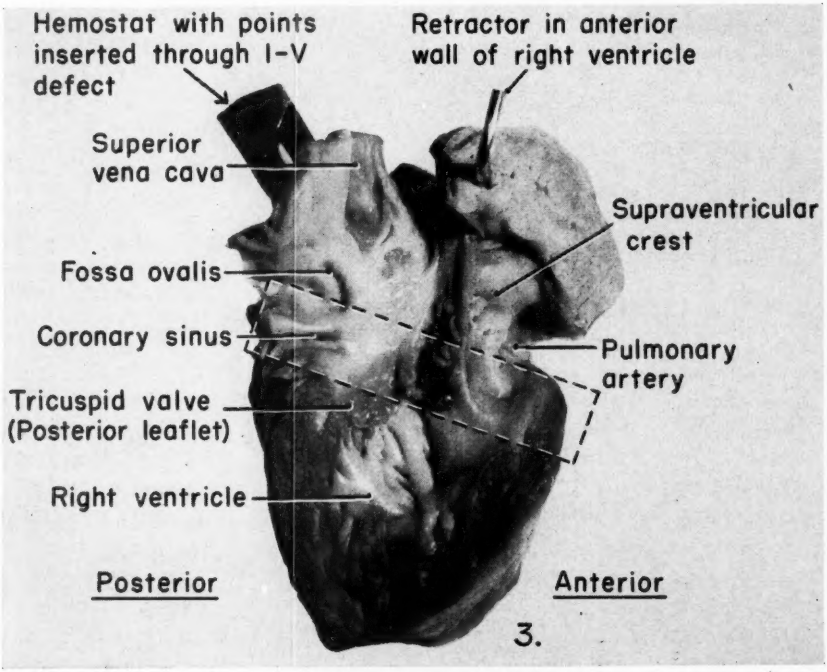

Fig. 3.—Interior view of right atrium and right ventricle of Specimen 2. The dotted rectangular area represents the region from which a wax model was reconstructed to demonstrate the location of the common bundle and its left and right branches. Compare with Fig. 7, *A*.

The microscopic appearance and relations of the common bundle are shown above the fibrous ring in Fig. 4, and as the bundle passed through this connective tissue layer at the atrioventricular junction in Fig. 5. The common bundle is identified below the fibrous ring as it lies in the free posterior margin of the interventricular septal defect (Fig. 5). Distally, the common bundle divided on the postero-inferior margin of the defect (Fig. 6) into a broad flat left bundle branch and a smaller right bundle branch. The relations of the microscopic right and left bundle branches to the defect (Fig. 6) are easily seen by comparing the microphotographs with the same structures in Fig. 7.

In view of the well-stained specialized muscle fibers, it was deemed desirable to demonstrate the crucial three dimensional relations of the conduction system in this specimen by means of a wax model reconstruction. Serial sections were projected and traced from the region of the atrioventricular node above, to the formation of the 2 bundle branches below. The region of the heart thus reconstructed by means of superimposed wax plates is indicated by the dotted rectangular area shown in Fig. 3.

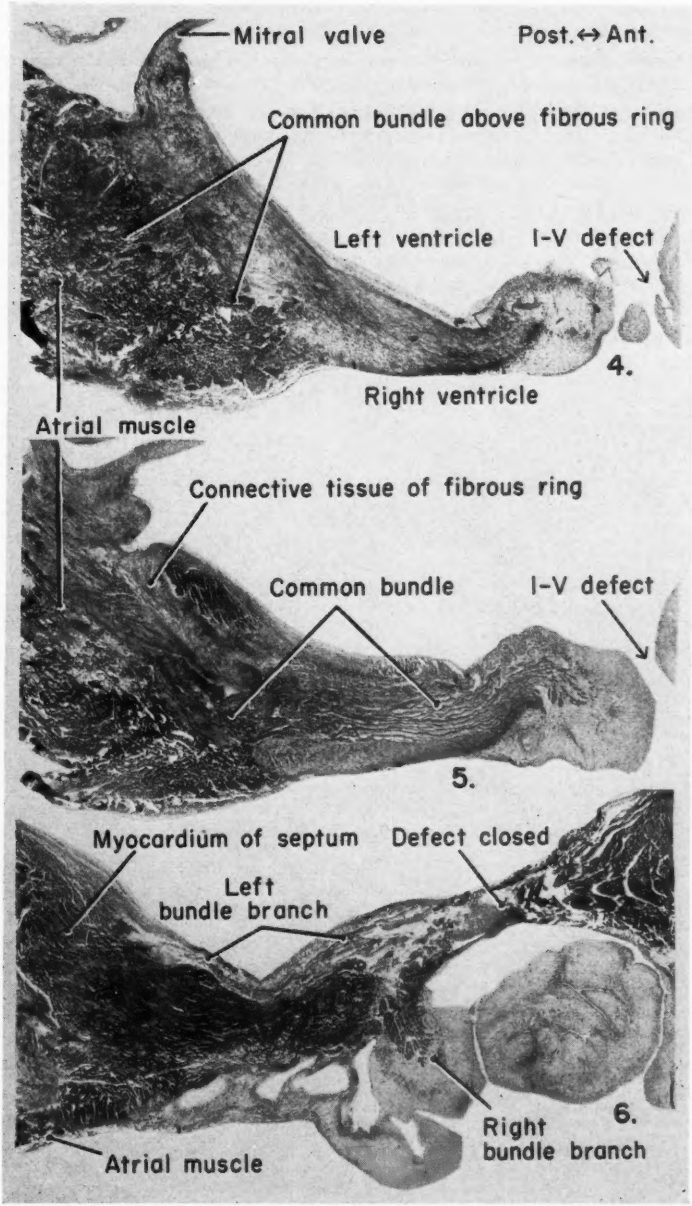

Fig. 4.—Microphotograph of a section of Specimen 2. Note the atrial position of the common bundle to the I-V defect before it passed through the fibrous ring. (Masson technique, ×25; reduced ⅔.)

Fig. 5.—Microphotograph of Specimen 2 illustrating the relationships of the common bundle to the defect, as it crossed the fibrous ring (annulus fibrosus). (Masson technique, ×25; reduced ⅔.)

Fig. 6.—Microphotograph of Specimen 2 at the lower margin of the I-V defect as it closed. The common bundle (Fig. 5) has just divided into a thin left bundle branch and a more compact right bundle branch. For orientation of Figs. 4, 5, and 6 see Figs. 3 and 7. (Masson technique; ×25; reduced ⅔.)

The close proximity of the common bundle to the postero-inferior margin of the septal defect is well shown by this reconstruction (Fig. 7, *A* and *B*).

In Fig. 7, *B* the origin and initial course of the left bundle branch can be observed as it passed distally under the septal endocardium of the left ventricle. Just below its origin, the left bundle branch divided into a large anterior division and a smaller posterior division. When the right ventricular surface is viewed (Fig. 7, *A*), the smaller right bundle branch can be observed as it courses anteriorly below the lower margin of the defect.

The dotted line in Fig. 7 indicates the location of the fibrous atrioventricular ring (annulus fibrosus). As illustrated in this model not all of the pale stained muscle fibers of the common bundle passed through the fibrous ring. A large mass of residual tissue remained on the right atrial side of the fibrous ring and formed the fingerlike ridge of tissue identified as an aberrant branch of conduction tissue in Fig. 7, *A*. From this aberrant

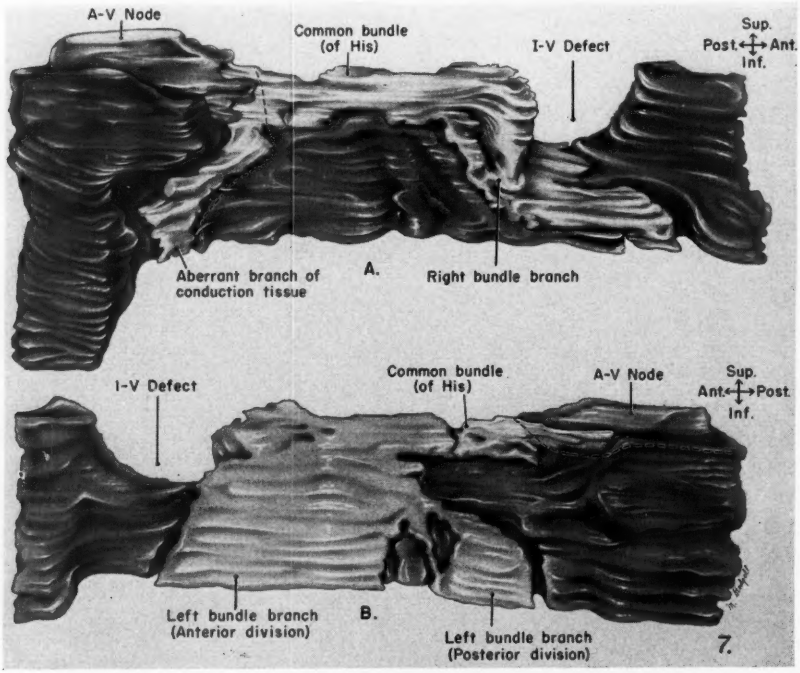

Fig. 7.—Drawing of a wax model reconstructed from the dotted area indicated in Fig. 3. The relations of the conduction tissue elements to the I-V defect are shown as viewed from the right ventricle in *A*, as viewed from the left ventricle in *B*. Note the position of the common bundle and its 2 branches to the postero-inferior margin of the defect. A large mass of pale stained fibers remained in the right atrium after the common bundle had passed through the fibrous ring (dotted line). Two small fascicles of fibers extended from this aberrant conduction tissue (Fig. 7, *A*) through the fibrous ring, and into the myocardium of the interventricular septum (i.e., bundles of Kent).

ridge we were able to follow 2 slender twigs of pale stained fibers across the fibrous ring and into the posterior part of the interventricular septum. Distally, the remainder of this aberrant tissue broke up into smaller fascicles, and they in turn were lost within the connective tissue of the fibrous ring.

Not shown in Fig. 7 was a larger mass of such residual tissue that remained proximal to the fibrous ring nearer the atrioventricular node. This "left-over" bundle tissue crossed the

fibrous ring at a lower level, to send fibers into the lower surface of the common bundle as well as into the top of the muscular interventricular septum posterior to the defect. A few muscle fibers were noted in the base of the posterior leaflet of the tricuspid valve in this specimen, but they had no relation to the myocardium of the interventricular septum or right ventricular wall.

Specimen 3. (No. A 549, white female, age 2 months.)

In addition to a high I-V defect, this specimen had a markedly dilated right atrium, patent foramen ovale, completely stenosed pulmonary artery, aorta overriding the I-V defect, and tremendous hypertrophy of both the left and right ventricular walls. The microscopic sections also demonstrated extensive hemorrhage within the atrioventricular node, common bundle and small left bundle branch.

This heart, like Specimens 6 and 8, demonstrated numerous variations of the conduction tissue. As shown in Fig. 8 this heart had an aberrant fascicle of specialized tissue that arose from the common bundle as it passed through the fibrous ring. This aberrant fascicle passed anteriorly above the defect and then descended in front of it. The remainder of the common bundle passed deep to what appeared to be a thickened crista supraventricularis and then coursed inferiorly in the posterior margin of the I-V defect. As the common bundle descended to the lower margin of the defect, it gave off a very small left bundle branch which traversed the top of the septum to reach the endocardium of the left side (Figs. 8 and 9). The small left bundle branch (Fig. 9) could be followed for only a short distance before it was lost within the muscle fibers of the septum due to hemorrhage and the poorly differentiated bundle tissue.

A small bundle of Kent was observed to connect the right atrium with the posterior portion of the interventricular septum. A separate bundle of fibers issued from the common bundle to descend and become lost within the septal myocardium posterior to the defect. The presence of these septal strands may account for the small size and composition of the left bundle branch in this specimen.

Specimen 4. (No. A 4752, Negro female, age 3 months.)

This heart had a transposition of the aorta as well as a very large anteriorly placed I-V septal defect. As demonstrated in Figs. 10 and 11 the transposed pulmonary artery was markedly dilated, whereas the aorta was of smaller diameter and possessed a thinner wall.

It will be noted in Figs. 10 and 11 that the common bundle, after crossing through the fibrous ring, descended posterior to the defect and was located under the endocardium on the left side of the heart. While in this left posterior position the common bundle divided into its left and right bundle branches at the point indicated by the black dot in Fig. 11. Both the left and right bundle branches were unusually small. The left bundle branch then continued distally as a broad but very thin band of fibers (Fig. 11). The smaller right bundle branch was followed as it traversed and descended from left to right within the myocardium of the upper interventricular septum (Fig. 10). A short distance below the lower margin of the defect the right bundle branch reached the right endocardial surface of the septum and gave off several rami.

The small size of the 2 bundle branches may be explained in part by the existence of 2 rather large accessory muscle bundles. The latter extended from the common bundle above the fibrous ring, to the cardiac musculature of the I-V septum posteriorly. The course of these 2 accessory pathways as they descended behind the tricuspid valve is shown by the arrows in Fig. 10.

Specimen 5. (No. A 5449, white male, age 5 months.)

This specimen also demonstrated a transposition of the great vessels, stenotic pulmonary artery, and a very large patent foramen ovale. The small left atrium appeared to be only an expanded terminus for the small pulmonary veins. A large high interventricular defect was placed anteriorly.

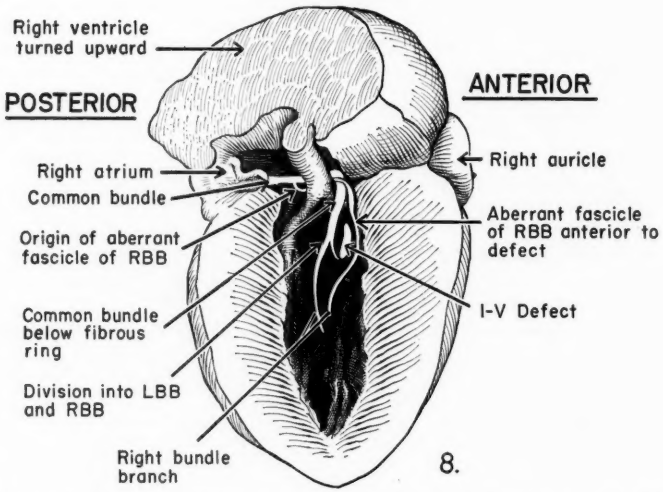

Fig. 8.—Drawing of the interior of the right atrium and ventricle of Specimen 3. The relations of the common bundle and its branches to the defect are indicated. Note the long slender aberrant fascicle of the right bundle branch (*RBB*) as it passed above and then descended anterior to the defect.

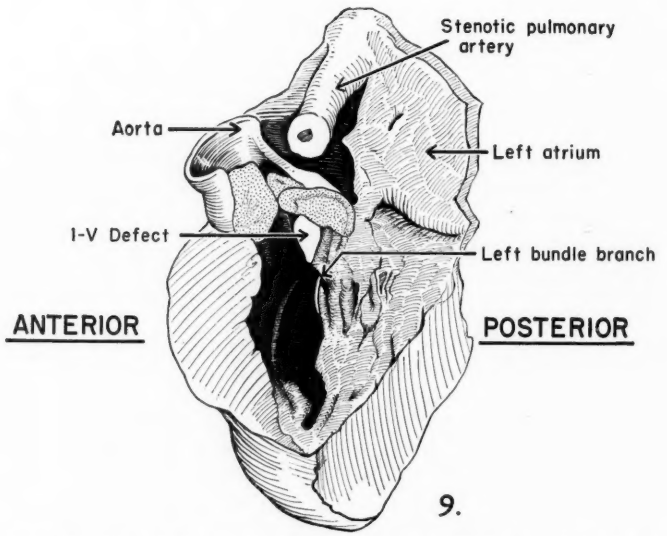

Fig. 9.—Drawing of the interior of the left ventricle of Specimen 3. The thin left bundle branch was extremely small in this heart (see text).

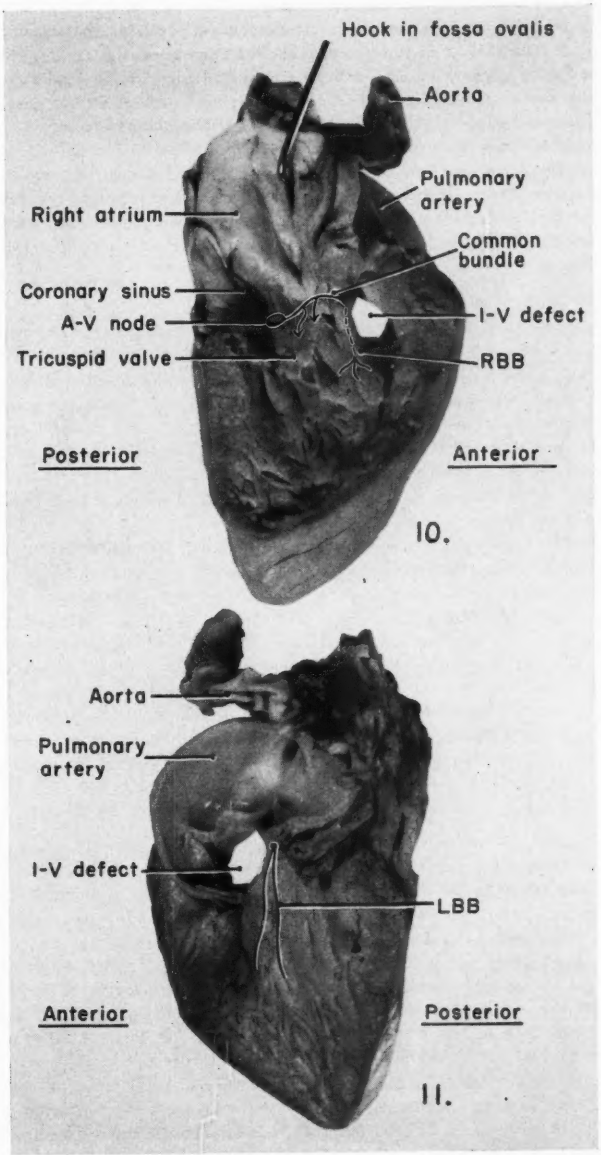

Fig. 10.—Interior of the right atrium and ventricle of Specimen 4. The intramyocardial course of the right bundle branch (*RBB*) is dotted. The arrows indicate the origin and course of 2 accessory pathways between atrium and ventricle (i.e., bundles of Kent).

Fig. 11.—Interior of left ventricle of Specimen 4. The common bundle divided (black dot) on the left side of the heart and posterior to the I-V defect.

The common bundle of conduction tissue in this specimen had a distribution quite similar to that shown in Figs. 1 and 2. It descended posterior to the septal defect, and divided into its 2 branches at the postero-inferior margin of the defect. The left bundle branch immediately assumed a flat, ribbon shape and gave off several rami to the upper portion of the septal myocardium as it descended in the endocardium on the left side of the heart. The small round right bundle branch was within the cardiac muscle as it descended on the right side of the septum (i.e., deep to the endocardium).

Although the distribution of the conduction tissue in this case was similar to that shown in Specimen 1, the present case had no rami that ascended anterior to the defect. However, as the common bundle divided into its 2 bundle branches, we could again trace several small fascicles from the lower end of the common bundle directly into the top of the interventricular septum.

Specimen 6. (No. A 6253, white male, age 6 months.)

This specimen had a large more inferiorly placed septal defect, transposition of the great vessels, and a patent foramen ovale.

There was a very small common bundle in this specimen. It was located under the endocardium on the left side of the septum. It descended and also divided into its terminal branches in the connective tissue above the septal defect. Both the left and right bundle branches were small, and both descended anterior to the septal defect near the junction of the anterior walls of the left and right ventricles. This is the only specimen studied microscopically in which both bundle branches descended anterior to a septal defect. An accessory bundle of Kent was also present in this specimen.

We observed numerous fascicles of large pale muscle fibers surrounding the transposed pulmonary artery. These fibers were similar to those found in the small common bundle. From this periarterial position we were able to follow this mass of pale fibers downward behind the defect into the endocardium of both the right and left sides of the interventricular septum. Below the I-V defect these fibers joined, and were incorporated with, the fibers of the left and right bundle branches. We were not able to establish histologic continuity proximally between the atrioventricular node and the mass of fibers observed around the transposed pulmonary artery. This was most unfortunate for we believe these periarterial pulmonary fibers were also a part of the conduction system and probably account for the small number of pale specialized fibers observed in the common bundle and the left and right bundle branches.

Specimen 7. (No. A 6256, Negro male, age 7 months.)

In addition to 2 I-V septal defects this specimen also demonstrated transposition of the great vessels, a patent foramen ovale, patent ductus arteriosus, and one large coronary artery that gave origin to the left and right coronary arteries.

The common bundle crossed the fibrous ring and descended posterior to both septal defects. As the common bundle descended it was located under the endocardium on the right side of the septum and it divided into its 2 bundle branches while in this position. At its origin from the common bundle, near the lower posterior margin of the defect, the left bundle branch then coursed through the upper myocardium to reach the left side of the septum, as shown in Fig. 12. The left bundle became a flat band of fibers as it descended and provided several rami that penetrated the musculature of the septum.

The smaller right bundle also gave origin to several early branches to the right side of the septum as it passed under the lower margin of the most posterior defect. A few small branches were seen to arise from the common bundle below the fibrous ring, prior to the origin of its 2 bundle branches. No accessory pathways were observed to connect the common bundle above the fibrous ring, with the interventricular septum below.

Specimen 8. (No. A 5466, white male, age 7 months.)

This heart demonstrated a small anteriorly placed I-V defect, transposition of the great vessels, and a patent foramen ovale. The common bundle divided into left and right bundle branches immediately above the fibrous ring in this heart.

The left bundle branch descended posterior to the defect under the endocardium on the left side of the heart. It was located in the position normally occupied by the common bundle. Several rami were observed to leave the left bundle branch and enter the myocardium of the interventricular septum in the region of the defect.

The aberrant right bundle branch crossed the fibrous ring as 2 separate fascicles which entered the top of the septal myocardium. These 2 bundles never came to lie in the endocardium on the right side of the heart, but descended within the superficial part of the septal myocardium and were soon lost as discrete bundles. Although several pale stained fiber bundles in this specimen were traced into the fibrous ring, no accessory muscle bands were seen to cross the ring to connect the atrium above with the septum below.

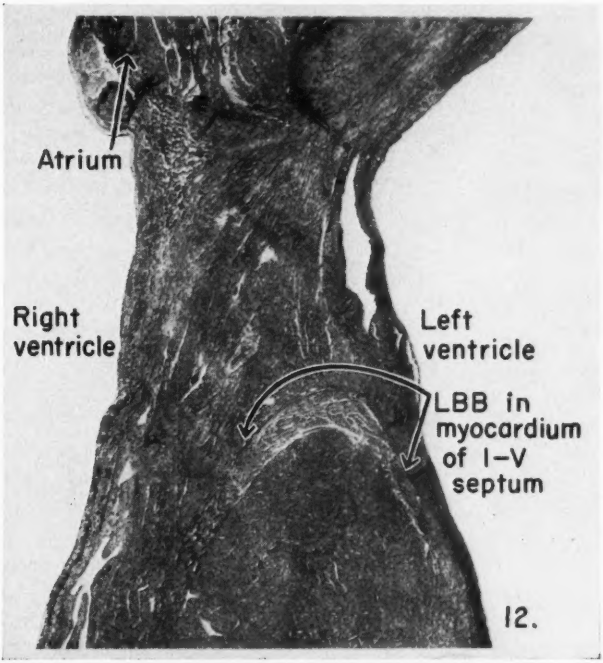

Fig. 12.—Microphotograph of a coronal section through the interventricular septum posterior to the 2 I-V defects of specimen 7. The common bundle divided under the endocardium on the right side of the septum. The left bundle branch (*LBB*) is shown as it coursed through the myocardium of the I-V septum to reach the endocardium on the left side of the heart. (Hematoxylin and eosin technique; ×40; reduced ⅓.)

Specimen 9. (No. A 54-51, white male, age 3 years.)

As illustrated in Figs. 13 and 14 this heart had a large high I-V defect, transposition of the great vessels, a dilated aorta that overrode the defect, and a stenosed pulmonary artery.

The common bundle again passed posterior to the defect, and after crossing the fibrous ring came to lie under the endocardium on the left side of the septum (Figs. 13 and 14). At the postero-inferior margins of the I-V defect the hemorrhagic common bundle divided (*x* in Fig. 14). As the left bundle branch continued distally, the right bundle branch coursed through the septal myocardium to gain the endocardium on the right side (Fig. 13). We again observed a strand of fibers leaving the common bundle as it divided. These fibers plunged immediately into the myocardium of the I-V septum posterior to the defect (arrow in Fig. 14).

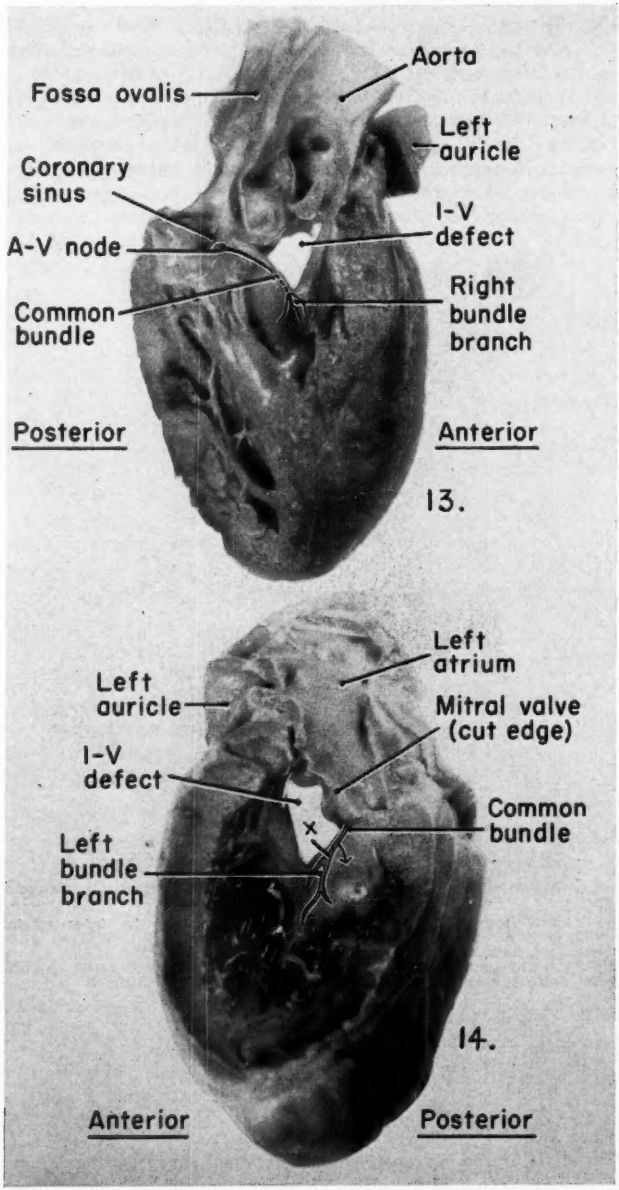

Fig. 13.—Interior of right atrium and ventricle of Specimen 9. The common bundle divided in the endocardium on the left side of the heart. Note the intramyocardial course of the right bundle branch (dotted) as it descended posterior to the defect.

Fig. 14.—Interior of left atrium and ventricle of Specimen 9. Note course of the common bundle as it passed deep to the cut edge of the mitral valve. The *X* marks the point of division of the common bundle into its 2 branches. The arrow indicates the origin and course of a fascicle of conduction fibers from the common bundle to the top of the interventricular septum (Mahaim's fibers).

Specimen 10. (No. A 6254, white female, age 27 years.)

In addition to 2 small I-V defects, this heart had a very large interatrial septal defect.

In this last specimen studied microscopically, the common bundle again descended posterior to both I-V defects. At the lower margin of the more posterior defect, the common bundle divided into 2 well-differentiated bundle branches. The left and right branches gave rami to the septal myocardium as they descended in the endocardium of the left and right sides of the heart. No accessory muscle bundles were observed to connect the atrial and ventricular myocardium in this specimen.

Description of Dissected Specimens.—With the aid of a dissection microscope, the superficial layer of endocardium was partly removed to expose the regions of the atrioventricular node, common bundle and left and right bundle branches. Small pads of fat and connective tissue strands were removed in the area from the level of the coronary sinus above to the fibrous ring below. When viewed with moderate magnifications (i.e., ×5 to ×15), the fibers of the conduction tissue appeared white and pale in contrast to the red of the regular cardiac muscle and yellow appearance of the fat. In formalin-fixed material the regular myocardial fibers are yellow to brown, whereas the conduction elements are white and delicate. Engorged venous channels were also identified in the atrial regions of the conduction tissue above the fibrous ring. However, the course and relations of the vascular channels were most conspicuous in fresh, unfixed specimens.

In 4 formalin-fixed specimens (Specimen 13 excluded), we could identify the left bundle and its ramifications in the endocardium of the left ventricle with minimal dissection. For this reason the left bundle branch was exposed first, then the atrioventricular node, common bundle and right bundle branch. The latter was the most difficult structure to demonstrate due to its small caliber, acute angular course, and early branching. A similar procedure was followed in each of the dissected specimens with highly satisfactory results.

Specimen 11. (No. A 2082, white female, age 3 days.)

This heart possessed a high I-V defect, 4 mm. in diameter. The atrioventricular node was a discrete ovoid swelling located below the orifice of the coronary sinus, and 1.5 mm. above the fibrous ring. The common bundle was a rounded mass of fibers that coursed inferiorly through the fibrous ring, and turned anteriorly to reach the connective tissue, posterior to the defect. In this position it divided into left and right bundle branches similar to the illustrations of Specimen 12 (see Figs. 15-18). The right bundle branch descended 2 mm. posterior to the defect on the right side of the septum and was soon lost as a discrete branch. The left bundle branch was a very thin sheet of fibers in the posterior margin of the defect. It reached and spread out over the myocardial fibers of the septum between 4 and 5 o'clock as the heart was viewed from the left side.

Specimen 12. (No. A 8506, white male, age 6 weeks.)

In addition to a high septal defect 8 mm. in diameter, this specimen had a patent foramen ovale and hypertrophy of the left ventricle. The gross topography of this heart and the location of the defect prior to dissection are illustrated in Figs. 15 and 17. As shown in Fig. 18, the atrioventricular node possessed a small inferior branch that extended deep and to the right along the upper surface of the fibrous ring. The stout common bundle divided at the posterior margin of the defect into its 2 branches. The thin right bundle branch (*RBB* in Fig. 18) descended for only a short distance on the right side of the septum and was soon lost in the endocardium.

The left bundle branch (*LBB* in Fig. 16) was an ovoid funiculus at its origin, but rapidly broadened into a flat bundle that spread out superficial to the myocardium of the septum. Many smaller fascicles of conduction fibers could be observed through the endocardium as they coursed distally from the parent left bundle branch.

Specimen 13. (No. A 54-222, Negro female, age 3 months.)

This specimen was essentially a heart with a common atrioventricular canal. In addition to an atrioventricular defect that measured 12 by 9 mm., there was a patent ductus arteriosus.

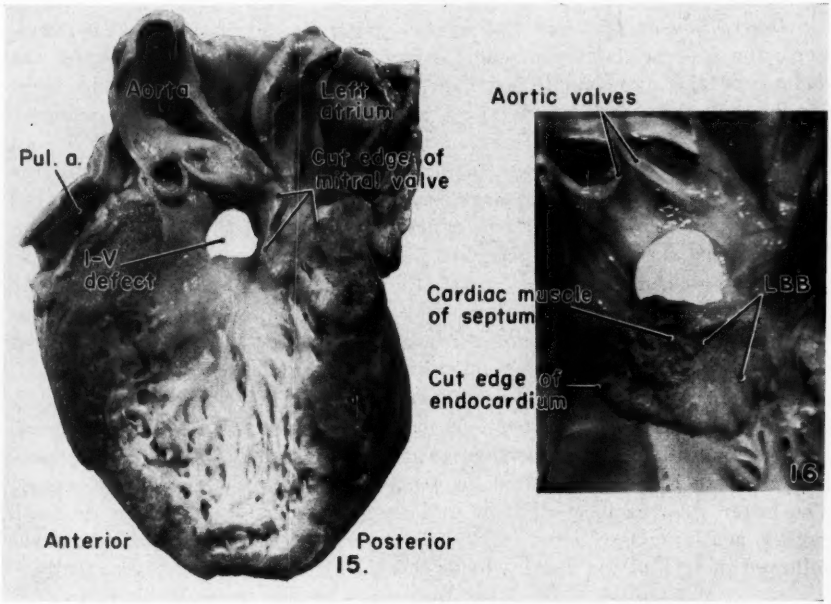

Fig. 15.—Interior of the left atrium and ventricle of Specimen 12. The I-V defect and topographic landmarks are identified.

Fig. 16.—Enlarged dissected area of left ventricle from the same specimen shown in Fig. 15. Note the gross course and position of the exposed left bundle branch (*LBB*) to the high I-V defect.

The atrioventricular node was a discrete ovoid mass. The common bundle passed through a tough mass of connective tissue as it coursed anteriorly to reach the posterior margin of the defect. Within this thick fibrous margin it gave origin to its branches.

The thin right bundle divided promptly into 2 smaller rami that descended on the right side of the septum. A small anterior ramus coursed anteriorly below the defect to attain the base of the papillary muscle of the conus, whereas a larger ramus descended more posteriorly on the septum. The thick left bundle branch plunged immediately into the myocardium at the top of the septum, and only a few fascicles could be identified in the endocardium on the left side of the septum.

Specimen 14. (No. A 9-53, white male, age 4 months.)

This was the only specimen that had a high septal defect located far *posteriorly.* The defect was only 2 mm. in diameter. This specimen also demonstrated a patent foramen ovale.

The atrioventricular node and common bundle were discrete structures and normally located within the right atrium. After passing through the fibrous ring, the common bundle

divided almost immediately into its 2 well-defined bundle branches at the lower margin of the small membranous portion of the I-V septum. The point of division was 10 mm. above the base of the papillary muscle of the conus, and 8 mm. above and anterior to the small septal defect. Both the left and right bundles passed anterior to the defect as they descended on the left and right sides of the septum.

Specimen 15. (No. A 2-48, white female, age 10 months).

A large defect 6 by 8 mm. was located posterior to the supraventricular crest, and opened into the right ventricle behind the medial cusp of the tricuspid valve. This heart demonstrated a patent foramen ovale and dilated aorta.

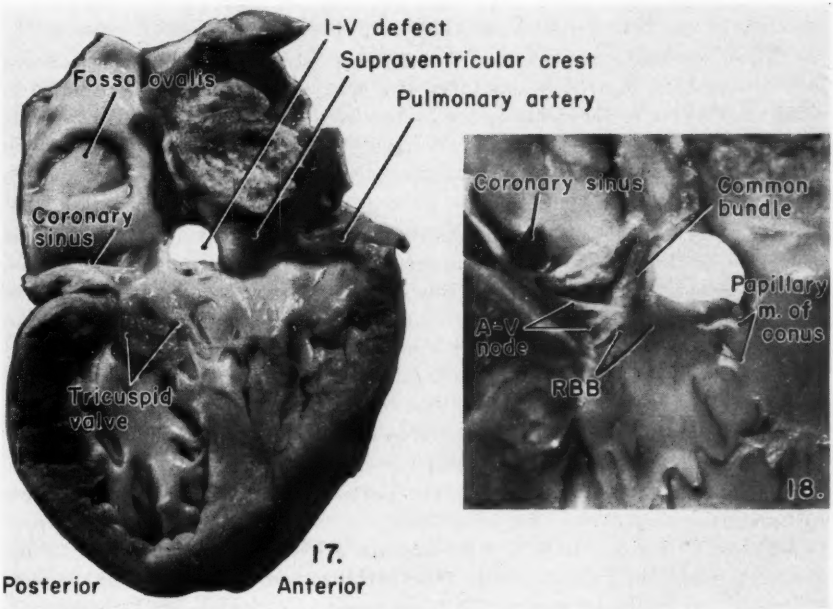

Fig. 17.—Interior and topography of the right atrium and ventricle of Specimen 12.

Fig. 18.—Enlarged area of dissection to demonstrate the location and appearances of the atrioventricular node, common bundle and right bundle branch. Same specimen shown in Fig. 17. The remainder of the tricuspid valve and part of the endocardium were removed to expose the conduction elements.

A well-defined atrioventricular node and common bundle were identified in the normal atrial position of this heart. The common bundle was traced through the fibrous ring to its division in the middle of the posterior margin of the defect. The origin and course of its 2 branches were very similar to those of Specimen 12 (see Figs. 15-18). The right bundle branch was quite large, and descended in the free postero-inferior margin of the defect to reach the myocardium of the septum. Although the left bundle branch was only slightly larger than the right bundle it assumed the shape and appearance similar to the bundle illustrated in Fig. 16.

DISCUSSION

The results of the present investigation have demonstrated the position and branching of the common bundle (of His) along the postero-inferior margin of interventricular septal defects in 8 of the 10 human specimens

studied microscopically. It occupied a similar position in 4 of 5 hearts prepared under a dissecting microscope. This intracardiac relationship corroborated a preliminary demonstration,[10] and verifies the "presumed location of the conduction system" as illustrated by Kirklin and his co-workers.[6] Although all of the conduction tissue descended anterior to the defect in Specimen 6, and only a portion of it in Specimen 3, it should be recalled that additional fibers of the conduction system were present in both cases. In the former, we observed numerous aberrant fibers about the transposed pulmonary artery, while in Specimen 3 (see Figs. 8 and 9) the main portion of the common bundle and both bundle branches were posterior to the defect.

Thus, it would appear that these anteriorly placed conduction fibers would have been injured by ligatures, if a surgical attempt had been made to close the defects in these specimens by reported techniques.[4, 5, 8] However, it is doubtful that such damage would have caused a complete heart block in either case, in view of the more posteriorly placed branches of the conduction system.

It is worthy of special emphasis that Kirklin[6] has called attention to the presumed location of the conduction system in the inferior angle of the defect. He also noted that by protecting this area during recent surgical closure of septal defects in 25 patients, they had encountered no heart block. However, in an earlier series, 3 cases of heart block had resulted in 10 or 11 patients before they took the precaution of protecting the posterior and inferior margins of such septal defects. We believe the reason for the absence of heart block in Kirklin's revised surgical approach is explained by the anatomic findings reported in the present communication.

As one grossly examines such septal defects on the left side of the septum, as though looking at the face of a clock, the conduction tissue would appear to be most vulnerable to injury by ligature between 1 and 6 o'clock. When viewed through the right ventricle, this specialized muscle tissue would be most vulnerable to injury by ligature between 6 and 11 o'clock. To the best of the authors' knowledge no one knows just how much of the ventricular conduction system must remain intact to prevent complete heart block. One finds considerable speculation on this point, and the final answer must take into consideration the early rami that pass directly into the myocardium of the interventricular septum from the common bundle, prior to its division into left and right bundle branches. Such early branches from the common bundle after it passed through the fibrous ring were noted by Mahaim,[17] and called "parasecific conduction fibers." In the present study, such fibers were traced from the common bundle into the very top of the I-V septum in 7 of the 10 specimens (e.g., arrow in Fig. 14). In addition, small fascicles were seen to leave the left bundle branch near its origin and enter the septum in 4 specimens.

We were surprised also to find accessory muscular pathways (bundles of Kent[18]) connecting the common bundle above the fibrous ring with the septal myocardium below the fibrous ring (Specimens 2, 3, 4, and 6). These aberrant bundles are in addition to the common bundle (of His). They were also

observed microscopically in the hearts of patients who had manifested an ante-mortem Wolff-Parkinson-White syndrome by several recent investigators.[19-22] We observed no bundles of Kent in specimens that were beyond 6 months of age. It is obvious that such early branches of the common bundle, and the accessory pathways of Kent, become of paramount importance following surgical closure, particularly if the common bundle, or its left and right bundle branches, are injured or incarcerated by a ligature distally. Although one cannot predict their presence, absence, or number in a given heart, their anatomic identification here implies there might be a margin of safety in the event the common bundle or its branches were damaged distally.

It should be noted that the common bundle normally divided at the top of the I-V septum. In the present series this division occurred under the endocardium on the left side of the heart in 3 cases, and on the right endocardial surface in 2 other specimens.

Studies are now in progress in our laboratory on the degenerative and regenerative capacities of the conduction system. It is hoped that this work, as well as the physiologic approaches such as those of Scher,[23] and Scher and Young,[24] Draper and Weidemann,[25] and Coleridge and his colleagues[26] will throw additional light upon the physiology of the conduction system. More extensive pathologic studies similar to those of Yater and associates[15, 16] and Lev and Unger[27] are also necessary.

The presence of hemorrhage within the A-V node and bundle branches of 6 specimens is difficult to explain, inasmuch as no ante-mortem arrhythmias were noted. It is possible that such hemorrhage occurred as a result of venous congestion and agonal spasm at the time of death. Thin-walled veins and sinusoids from the myocardium are known to course through the conduction tissue,[28, 29] en route to the coronary sinus. These veins and sinusoids were engorged with blood in most of the specimens in the present series. One can also identify these vascular structures while dissecting above the fibrous ring in fresh unfixed hearts.

Final brief mention should be made concerning the location of the conduction system during the development of the heart. Walls,[11] in an excellent study of human embryos, has pointed out that these specialized fibers appeared to be related to the posterior wall of the atrioventricular canal. The posterior location of this specialized system in most of our anomalous older specimens would support Walls' belief. This was impressed upon us particularly as we exposed the incarcerated common bundle of Specimen 13. In this case the entire postero-inferior margin of the atrioventricular defect was a thickened, tough, fibrous mass of connective tissue that encased the common bundle. We cannot say whether this represented a portion of the arrested remains of the dorsal endocardial cushion.

Further study of the development of the conduction system in younger human embryos is now being undertaken in this laboratory. We hope that the results of this newly initiated program will extend the observations of Walls,[11] and provide information for some of the present unanswered questions.

SUMMARY

The position, course, and variations of the cardiac conduction system were studied in 15 human hearts with high interventricular septal defects. Ten specimens were studied by serial microscopic sections while the conduction elements were demonstrated grossly in 5 hearts with the aid of a dissecting microscope.

In 12 specimens the common bundle as well as the left and right bundle branches were located in the postero-inferior margin of the septal defect. These important relations of the conduction system are illustrated by means of photographs, drawings, and a wax model reconstruction. It is essential that the posterior margin of such high septal defects be protected from sutures and strong traction during surgical closure if complete or partial bundle branch blocks are to be avoided.

The common bundle divided into its 2 bundle branches above the fibrous ring in 1 specimen, and immediately above the septal defect in another (Specimens 8 and 6). The left and right bundle branches descended anterior to the defect in only 2 hearts (Specimens 6 and 14).

Accessory atrioventricular pathways of conduction tissue (bundles of Kent[18]) were demonstrated in 4 hearts. High branches from the common bundle (Mahaim's fibers[17]) into the top of the I-V septum were also noted in 7 of 10 specimens studied microscopically. The chief variations of the cardiac conduction tissue are presented as well as their physiologic and surgical significance.

Hemorrhage within the conduction tissue was observed in the microscopic sections of 6 hearts. Numerous, thin-walled, venous channels are known to traverse the conduction tissue en route to the coronary sinus and right atrium. Rupture of these endothelial channels during agonal spasm may account for the post-mortem hemorrhage and clinical absence of ante-mortem arrhythmia.

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VENA CAVA—PULMONARY ARTERY ANASTOMOSIS FOR VASCULARIZATION OF THE LUNG

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ONE of the most difficult and most interesting problem in modern cardiology is the surgical treatment of complex cardiac malformations in the "impaired pulmonary circulation" group. A survey relevant to this problem shows that despite the remarkable results obtained there is still much to be desired. The surgical management for certain pathologic cardiac conditions, such as the noncomplicated pulmonary stenosis, has been solved theoretically and technically. The direct vision repair of tetralogy of Fallot under certain conditions has become a reality. On the other hand, conditions, such as tricuspid atresia, still await effective therapy, and the same applies to certain types of tetralogy of Fallot when the stenosis involves the entire length of the right ventricular outflow tract or when the pulmonary artery is excessively hypoplastic or atretic.

The Blalock[1] operation, or its modification developed by Potts, Smith and Gibson,[2] restores function satisfactorily in numerous cases, but has the following disadvantages.

1. The "patent ductus" created artificially increases greatly the left ventricular output and places considerable strain on the heart.

2. In the presence of high-grade pulmonary stenosis and relatively slight aortic dextroposition with small interventricular septal defect, the stress upon the right ventricle is great because the right ventricle has to force blood through very small apertures in the direction of both great vessels. A subclavian–pulmonary or aorta–pulmonary anastomosis may result in an increase of pulmonary arterial pressure, which in turn makes it even more difficult for the right ventricle to express the blood through the narrowed pulmonary orifice. Thus, right ventricular failure may develop.

3. The blood supplied to the lungs by way of the anastomosis is mixed arterial and not venous; therefore, the efficiency of the anastomosis is reduced.

4. There is a tendency to endarteritis.

5. The technique is exceptionally complicated especially with children.

The above considerations caused us to look for a surgical method[3] which would eliminate the disadvantages outlined.

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In congenital heart disease with impaired pulmonary circulation, as in tetralogy of Fallot, a rich subpleural network of small veins in the hilus is formed. This venous network connects the pericardiophrenic and parietal venous systems with the pulmonary circulation forming a collateral circulation. It seems logical that these vessels transport venous blood which bypasses the right heart and flows directly into the lungs.[4] This clinical observation gave us the idea to elaborate the procedure by surgical anastomosis.

EXPERIMENTAL OBSERVATIONS

Mongrel dogs of both sexes were used. The operations were performed under endotracheal anesthesia. The chest was opened in the right third intercostal space anterolaterally. The pleura covering the superior vena cava was incised longitudinally and the vein freed in its entire length. The main branch of the right pulmonary artery was transsected and the peripheral stump was held in an atraumatic clamp. The superior vena cava was then ligated just superior to the azygos vein. Between the ligation of a second clamp, the vena

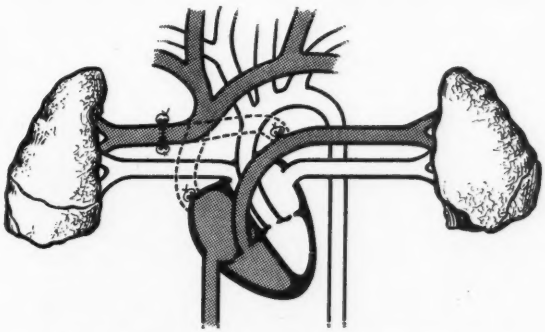


Fig. 1.—Schematic representation of the method.

cava was severed. The peripheral stumps of the transsected superior vena cava and the right main branch of the pulmonary artery were approximated by an end-to-end anastomosis. Upon removing the clamps, the right pulmonary artery readily filled from the superior vena cava. The azygos vein was ligated last and the chest was closed layer by layer (Fig. 1).

As a result of this operation, the venous blood flow is divided into two parts: the blood of the upper part of the body, which bypasses the right heart, flows from the superior vena cava directly into the right lung; the blood of the lower body flows "per vias naturales" through the right heart into the left lung (Fig. 2).

At 3- to 12-month intervals following the operation, the respiratory function and the hemodynamics were studied in the following manner.

The oxygen uptake was determined separately for the left and for the right lung by selective bronchospirometry. At the same time, an intravascular catheter was introduced into the right external jugular vein and passed directly

into the right pulmonary artery via the anastomosed superior vena cava. Another catheter was passed through the femoral vein into the inferior vena cava and then through the right heart into the left pulmonary artery (Fig. 3). Samples of blood taken from the catheters and by direct arterial puncture were analyzed for oxygen content by photometry. Detailed records were made of blood pressure.

The blood flow through the right and left lungs, respectively, was calculated on the basis of the Fick principle, according to the following equations.

$$F_{ll} = \frac{O_r}{C_{art} - C_{rpa}} .100 \quad (1)$$

$$F_{rl} = \frac{O_l}{C_{art} - C_{lap}} .100 \quad (2)$$

Pulmonary vascular resistances in the right and left lungs were calculated according to the following equations.

$$PVR_r = \frac{MP_{rpa} - MP_{cap}}{\left(\frac{F_{rl}}{60}\right)} .1 \times 332 \quad (3)$$

$$PVR_l = \frac{MP_{lpa} - MP_{cap}}{\left(\frac{F_{ll}}{60}\right)} .1 \times 332 \quad (4)$$

where

F_{rl} = right lung blood flow in ml./min.
F_{ll} = left lung blood flow in ml./min.
O_r = oxygen uptake of the right lung in ml./min.
O_l = oxygen uptake of the left lung in ml./min.
C_{art} = blood oxygen content in the systemic arteries in vol. %.
C_{rpa} = blood oxygen content in the right pulmonary artery in vol. %.
C_{lpa} = blood oxygen content in the left pulmonary artery in vol. %.
MP_{rpa} = mean blood pressure in the right pulmonary artery in mm. Hg.
MP_{lpa} = mean blood pressure in the left pulmonary artery in mm. Hg.
MP_{cap} = pulmonary "capillary" mean blood pressure in mm. Hg.
PVR_r = "pulmonary vascular" circulatory resistance in the right lung in dyn. sec. cm.$^{-5}$.
PVR_l = "pulmonary vascular" circulatory resistance in the left lung in dyn. sec. cm.$^{-5}$.
1.332 = conversion factor.

Angiocardiographic examinations were carried out by means of an intravascular catheter introduced into the superior vena cava. Thirty milliliters of a 70 per cent preparation of Joduron were injected through the catheter into the superior vena cava, and the passage of the contrast medium was followed by serial roentgenography.

Finally, the circulatory effect of (a) obstruction of the left main bronchus, and (b) obstruction of the left pulmonary blood flow were studied.

The purpose of these experiments was to control the function of the right lung anastomosed with the superior vena cava in the absence of the function of the normal (left) lung. These experiments were performed with the aid of double lumen catheters provided with inflatable cuffs introduced into the left main bronchus (series No. 1) and into the inferior vena cava above the level of the diaphragm (series No. 2).

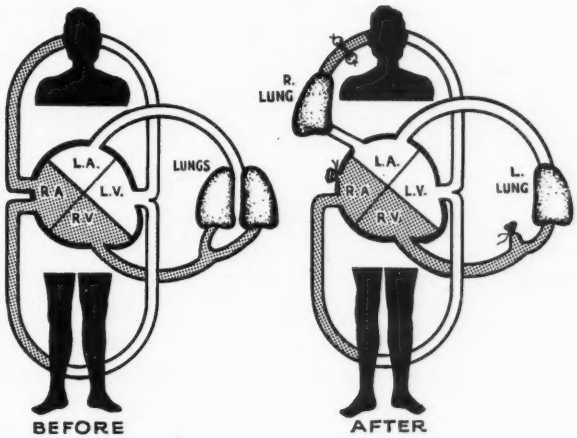


Fig. 2.—Schematic representation of the circulatory relations before and after the operation.

Fig. 3.—X-ray picture taken at the time of heart catheterization. The upper catheter is introduced through the superior vena cava direc ly into the right pulmonary artery. The lower catheter is introduced through the vena cava inferior and right heart into the left pulmonary artery.

RESULTS

End-to-end anastomoses between the superior vena cava and right pulmonary artery were performed in 30 dogs. Six dogs were lost in consequence of the operation. One died of empyema, one of heart fibrillation, 2 from obliteration of the anastomosis.

Twenty-two of the 24 survivors had patent anastomoses 3 months to 2 years after operation. One to 2 weeks after operation the behavior of the animals was

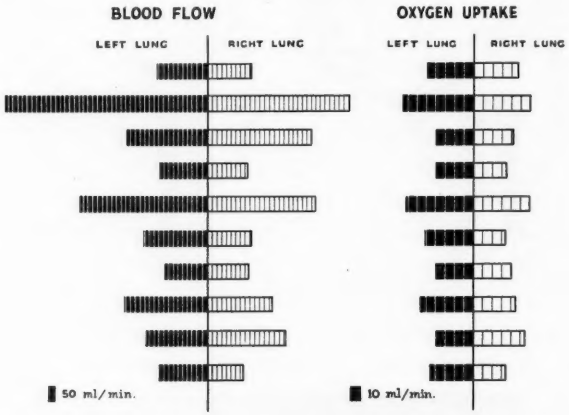


Fig. 4.—Pulmonary blood flow and oxygen uptake postoperatively of the right and left lungs.

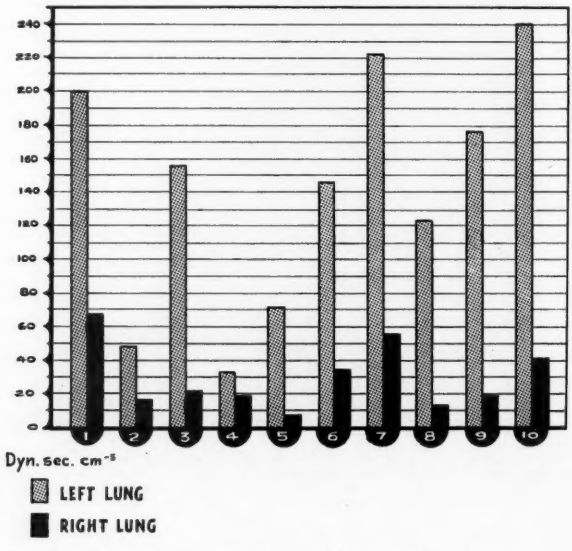


Fig. 5.—Pulmonary "vascular" circulatory resistance after operation.

normal. Half of this group was sacrificed 6 months after operation, the others were allowed to survive for further observation and examination.

At necropsy, the veins of the superior caval system were questionably larger. This was the only sign suggesting venous congestion. The vessels at the anastomotic site were patent and the suture line was completely covered by endothelium. There were no pathologic changes in the lungs histologically.

Bronchospirometry and hemodynamic studies were performed on 10 dogs. Relevant data on the respiratory function and the results of hemodynamic tests are summarized in Table I and Figs. 4, 5, 6, and 7.

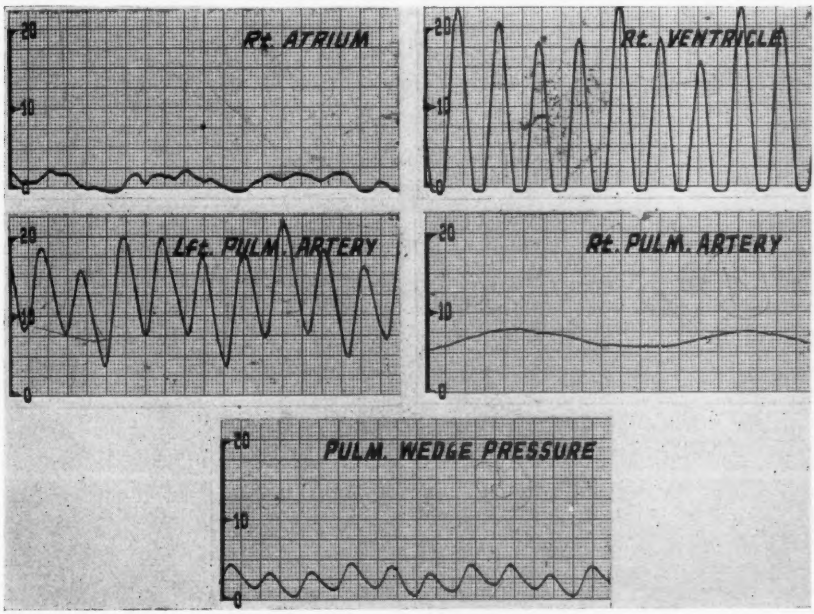
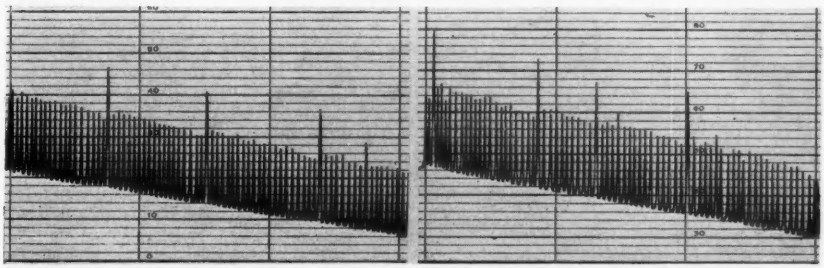


Fig. 6.—Postoperative pressure curves.



A. *B.*

Fig. 7.—Postoperative bronchospirometry. *A*, Right lung. *B*, Left lung.

Angiocardiographic examinations were performed on 6 animals. Serial roentgenography clearly showed the contrast material introduced into the superior vena cava filling the right pulmonary artery with its tributaries immediately (Fig. 8). The photograph taken one second later reveals normal parenchymal filling of the right lung. Two seconds later no contrast medium was detectable in the superior vena cava; the left heart and the aorta showed intensive concentration of the dye.

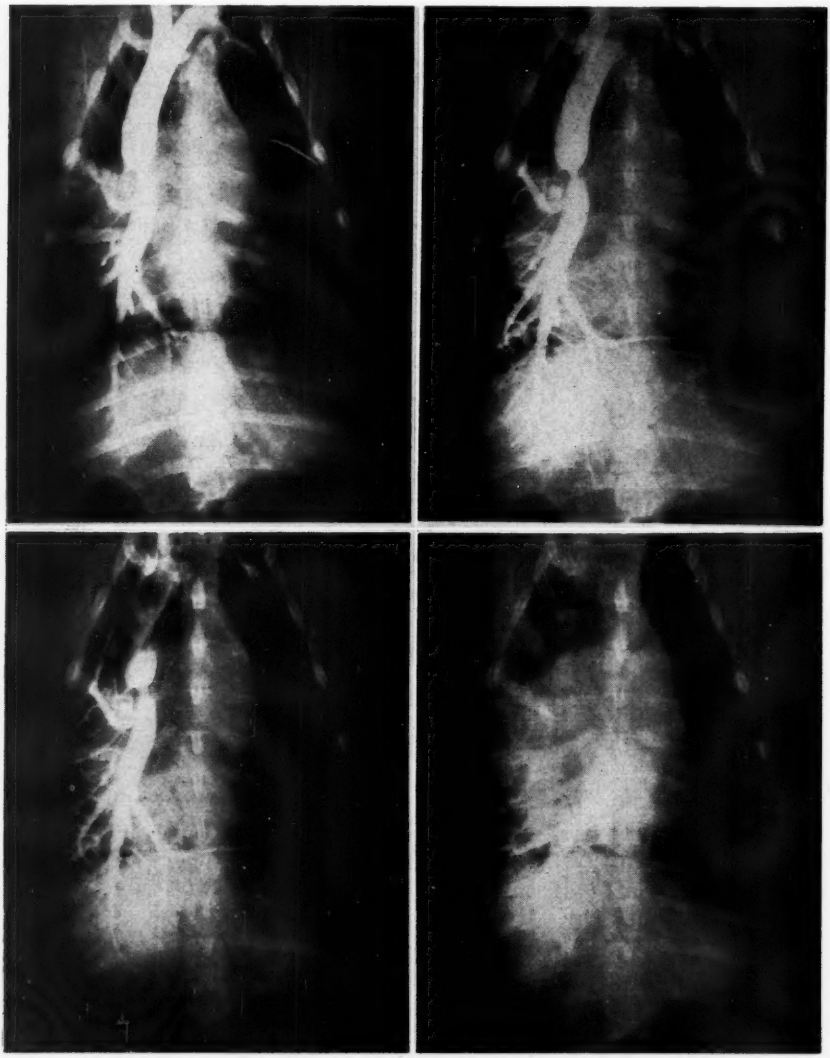


Fig. 8.—Postoperative angiocardiography.

The air passage of the left lung was obstructed in 5 dogs for 15 minutes, and the blood flowing into the left lung was also occluded for the same length of time. All dogs survived the 15 minutes of occlusion. The significant hemodynamic alterations in the group of the obstructed bronchus were slight elevation of the systemic arterial blood pressure, marked hypertension in the left lung and oxygen desaturation of the systemic arterial blood (Figs. 9 and 10).

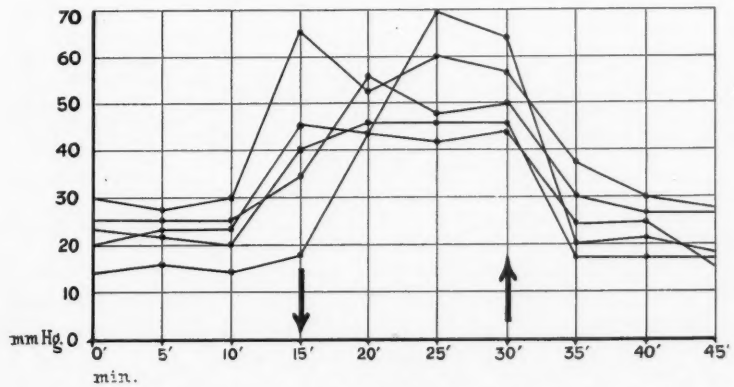


Fig. 9.—Systolic blood pressure in the left pulmonary artery. The arrows mark the beginning and the end of the obstruction of the left bronchus.

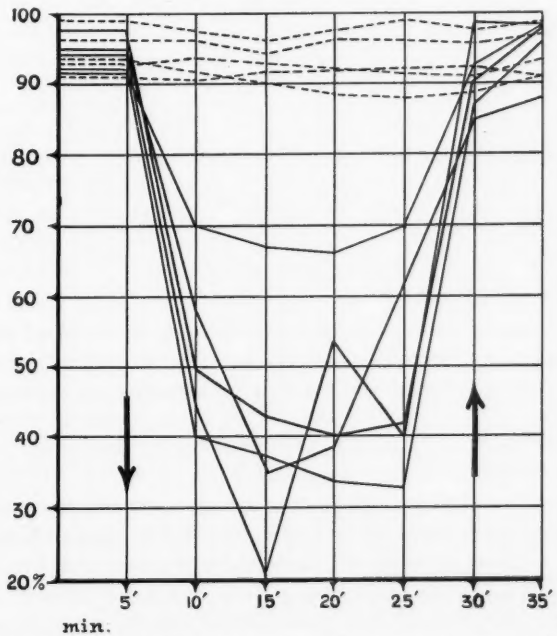


Fig. 10.—Oxygen saturation of the systemic arterial blood. The arrows mark the beginning and the end of the obstruction of the left bronchus (continuous line) or the left pulmonary blood flow (interrupted line).

In the group of obstructed left pulmonary blood flow, the only significant alteration was the decrease of the systemic arterial blood pressure. Oxygen desaturation of the systemic arterial blood did not develop.

TABLE I

NO.	BLOOD PRESSURES MM. Hg		
	VENA CAVA SUPERIOR	PULMONARY ARTERY	
		RIGHT	LEFT
1	7/2 (5)*	7/2 (5)	30/7 (15)
2	9/7 (8)	9/7 (8)	28/8 (18)
3	10/3 (7)	9/3 (6)	32/16 (20)
4	8/6 (7)	8/6 (7)	20/4 (8)
5	6/1 (4)	6/1 (4)	24/10 (14)
6	7/5 (6)	7/5 (6)	25/9 (16)
7	7/4 (6)	7/4 (6)	35/7 (15)
8	6/2 (5)	6/2 (5)	25/10 (14)
9	7/2 (5)	6/2 (4)	26/12 (16)
10	6/3 (5)	6/3 (5)	26/16 (18)

*Mean pressure.

DISCUSSION

In evaluating the results of our investigations and the efficiency of the method, the following points were considered.

A. *What are the technical difficulties of the method?:* Experience has shown that the operation does not involve any major difficulties technically. In the Blalock and Potts operations, the anastomoses are usually under tension. In the operation under discussion, the stumps of the two vessels are brought together with ease. This method can be carried out by any surgeon practiced in suturing blood vessels.

B. *What are the effects upon the pressure relations of the superior caval system?:* Although average blood pressure in the superior vena cava was a few mm. Hg higher than normal, this increase of pressure was not significant and caused no untoward symptoms. Two of the early experimental animals died in the first postoperative weeks as a consequence of the thrombosis at the anastomotic site. Excessive venous congestion and edema of the upper part of the body developed in these 2 dogs.

C. *Can the systemic venous pressure provide adequate blood flow through the lung?:* The above hemodynamic problem is one that ultimately decides whether or not the operation is practicable. It is known that the blood pressure is relatively low in the pulmonary circulation even in normal conditions and the pressure difference between the pulmonary artery and vein is no higher that 5 to 10 mm. Hg.[5, 6]

In conditions associated with pulmonary stenosis, the mean pulmonary arterial pressure is even lower (4 to 8 mm. Hg) and in spite of the small pressure difference between pulmonary artery and vein, the blood flow in cases of noncomplicated pulmonary stenosis does not decrease below normal values (Fig. 11). The cause of this may be the high adaptability of the vessels of the lungs.[7, 8] In support of this view, our experiments showed that pulmonary vascular

resistance was considerably lower at the site of the anastomosis than in the contralateral lung (see Fig. 5). It is believed that an active dilatation of pulmonary vessels (primarily in the arterioles) is the result of a reflex process.[9]

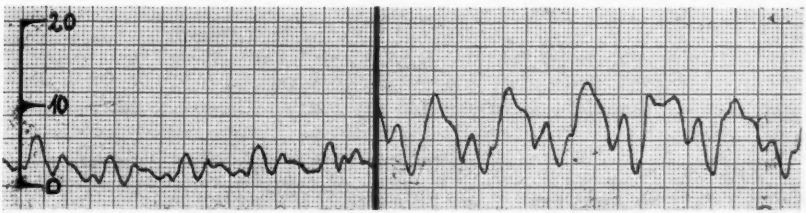


Fig. 11.—Blood pressure curve obtained by heart catheterization in pulmonary stenosis, (*A*) pulmonary vein, (*B*) pulmonary artery.

D. *Is the function of the lung attached to the systemic venous system equivalent to that of a normal lung?:* Hemodynamic studies showed nearly equal blood flow, and bronchospirometry revealed nearly equal oxygen uptake of both lungs (see Figs. 4-7). The right lung attached to the superior vena cava proved to be functioning satisfactorily. To check this function further biologically, we excluded the left lung from the respiratory process. Two different methods were used.

The first method was to prevent air getting into the left lung. We found that the obstruction of the left bronchus was followed by severe circulatory changes, i.e., pulmonary hypertension, significant cyanosis and desaturation of the systemic arterial blood (see Figs. 9 and 10). When the right lung is functioning normally, obstruction of the left bronchus does not produce such symptoms. On the first look we must suppose that the function of the right (anastomosed) lung of our experimental animals was impaired, but when we consider the specialties of the pulmonary circulation of our animals we must accept other suppositions. In the case of normal pulmonary circulation, when we obstruct the main bronchus of one lung, the blood flow of this lung suddenly diminishes because the rise in circulatory resistance directs the blood to the other lung.[10] It is the same situation in unilateral pneumothorax. However, when pulmonary circulation is divided into two separate parts, such is not possible. In spite of the reflex pulmonary vasoconstriction, which accounts for the hypertension in the left lung, the blood flowing from the inferior vena cava *must* flow through the left lung, as there is no other route. The desaturation of the systemic arterial blood and the cyanosis also must be seen as a consequence of a great veno-arterial shunt through the nonoxygenated left lung and not as a consequence of an impaired function of the right (anastomosed) lung.

This supposition was supported by a second group of experiments in which the function of the left lung was impeded by obstruction of the left pulmonary blood flow. It was found that, in spite of the fact that only the right lung was functioning, no signs of cyanosis or systemic arterial desaturation occurred (see Fig. 10).

E. *What is the effect of this method on the burden of the right ventricle?:* In congenital malformations associated with pulmonary stenosis, the narrowing of the pulmonary orifice places a great extra burden on the right ventricle. The work of the right ventricle can be expressed by the following equation:

$$W = Q.R \frac{mv^2}{2g}$$

where (W) is the work of the ventricle, (Q) represents the systolic discharge, (R) the mean pressure or resistance, (m) the mass of the ejected blood, and (v) the average velocity.[11] Because of the relative quantity, the $\frac{mv^2}{2g}$ is negligible.

The anastomosis created by the Blalock or Potts operations does not diminish the burden of the right ventricle. Contrarily in some cases, there is an elevation of the factor (R) pressure in the pulmonary artery. This increases the burden upon the right ventricular myocardium. The method being reported has no such effect. There is no elevation in the factor (R), but there is a great diminution of the systolic discharge (Q) of the right ventricle because the blood of the upper part of the body is shunted directly into the right lung.

F. *Is the method adaptable to the human being?:* At first glance, the operation described appears to be too hazardous to be recommended for use in human subjects. Nevertheless, it should be mentioned in connection with this problem that several operations now in use for the surgical treatment of congenital heart disease appeared to be fairly risky and complicated at first. Observations and experience in thoracic surgery show that the temporary clamping of one of the main branches of the pulmonary artery or the superior caval vein has no grave consequences even for the patient who is in poor condition.[12, 13]

SUMMARY

The authors developed experimentally a new method for the relief of certain congenital heart diseases associated with impaired pulmonary circulation. The essence of the procedure was as follows: the superior vena cava was transsected before entering the right atrium; the right pulmonary artery was severed at its origin with the main pulmonary trunk; the peripheral stumps of the two vessels were anastomosed by an end-to-end method. The right lung was thus supplied with blood directly from the superior vena cava. In this manner about half of the sytemic venous blood flow bypassed the right heart.

Animal experiments have shown that pulmonary blood flow and oxygen uptake are nearly equal on both sides. There is no significant increase in blood pressure in the area of the superior vena cava. The method as illustrated has advantages over other anastomotic operations in the following respects: (1) the operation places no extra burden on the heart; (2) blood pressure in the main trunk of the pulmonary artery is not increased; (3) this anastomosis supplies "pure" venous blood to the lung; (4) endarteritis is less likely to occur; and (5) technically the operation, even on small subjects, is not difficult.

Detailed physiologic changes, hemodynamics, and angiocardiography studies are reported.

The authors are indebted to Mrs. Ruth Crooks for valuable technical assistance.

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ANGIOCARDIOGRAPHY AS AN AID TO IDENTIFICATION OF NONRESECTABLE PULMONARY CARCINOMAS

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DEVELOPMENT OF ANGIOCARDIOGRAPHY AND ITS DIAGNOSTIC POTENTIALITIES

IN THE 18 YEARS since angiocardiography was first established as a clinical method by Robb and Steinberg,[5] much valuable work has been done in the evaluation of cardiovascular abnormalities, lesions of the mediastinum, and various forms of pulmonary pathology. Carcinoma of the lung has been one of the most recent major subjects to be so investigated, and the present discussion will deal with the accuracy of preoperative determination of its resectability.

The diagnosis of pulmonary carcinoma, and the role that angiocardiography may play in it will not be considered at this time. A number of writers[4] have devoted much effort to such studies and believe that angiocardiography plays a vital part in both the diagnosis and determination of resectability. The studies carried out at the Massachusetts General Hospital on the other hand confirm the opinion of Dotter, Steinberg, and Holman[3] and Amundsen and Sörensen[1] that, by angiocardiography, pulmonary carcinoma may be indistinguishable from certain other conditions and that its diagnosis must be established otherwise.

PREDICTION OF RESECTABILITY OF LUNG CARCINOMA

Certain clinical signs suggest that total resection may not be possible. These include phrenic or recurrent nerve paralysis, Horner's syndrome, cytologically positive pleural effusion, and distant metastases. Evidence of hilar or mediastinal extension, however, may not be apparent by conventional examination, either clinical or roentgenologic. Complete extirpation of carcinoma of the lung is impossible when it or its local metastases lie in intimate contact with vital intrathoracic structures which cannot be sacrificed. Principally these structures are the heart and great vessels. Involvement of the main right and left branches of the pulmonary artery, too close to the main trunk to permit resection, precludes removal of the tumor. Tumor invasion of the pulmonary veins close to the left atrium, or involvement by cancer of the superior vena cava prevents removal unless elaborate substitution of vessels is performed. Tumor lying in apposition with the aorta or great arteries to the head and arms may be resectable unless there be true invasion of these structures.

It is well known that most individuals with primary carcinoma of the lung are incurable when first seen. The figure varies with different authors but may run as high as 75 per cent. By presently accepted procedure, all patients are subjected to exploratory thoracotomy unless very obviously incurable

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because of local unresectability or metastases. This procedure is neither innocuous nor inexpensive and may result in postoperative morbidity or mortality. Exploration without resection produces needless discomfort. The patient deteriorating with extensive cancer rarely returns to preoperative level when he survives. Churchill and his co-workers[2] report a mortality rate of 10.6 per cent for exploratory thoracotomy in their series of cancer of the lung from 1933 to 1950. This figure has dropped considerably of late and is probably less than 2 per cent today. It has been with the hope of avoiding fruitless thoracotomies that this study has been undertaken.

The investigation has been concerned with the value angiocardiography may have as an aid to the recognition of certain nonresectable lung carcinomas. It had seemed probable that in centrally located tumors, especially, this procedure would be most useful. Even in the peripherally placed ones it may occasionally offer informative data concerning resectability by disclosing changes in the mediastinum or hilar structures. It has been our primary aim to determine the degree of accuracy of this prognostic measure.

The findings in a group of 23 individuals, all of whom had been submitted to preoperative angiocardiography, were checked at surgical operation. One of us (E. W. W.) was in attendance at 15 of the operations; detailed operative notes were available for review in all cases.

METHOD USED IN ANGIOCARDIOGRAPHY

Examinations were performed initially using the original method of Robb and Steinberg, namely a No. 12 cannula inserted into and tied in one of the deep arm veins through which was introduced a concentrated iodine compound. At first, 50 per cent Diodrast was used, but this has been replaced by 70 per cent Urokon. Serial films were made, originally by a homemade cassette-changing device which permitted 20 exposures at rates up to 3 per second, in one projection. More recently a biplane roll film changing device (Elema) has been employed providing simultaneous anteroposterior and lateral recording at rates up to 12 frames per second in each projection. Most examinations had been done at the rate of 6 frames per second for 2 or 3 seconds followed by 2 per second for an additional 5 or 6 seconds, and finally 1 per second for a total run of 15 to 20 seconds. The method of injection has also been changed, as experience dictated, using a No. 11 or 12 Lehman catheter introduced via the deep veins of the arm on the affected side into the corresponding innominate vein, and the compound injected by means of a central-bore Robb hand-operated syringe. The method has been quite satisfactory, permitting the introduction of between 50 c.c., and at the most 70 c.c., of 70 per cent Urokon in less than 2 seconds. This part of the procedure has been performed by the surgeon with the radiologist determining the proper positioning of the patient in addition to other radiographic factors. General anesthesia has not been needed or used although an anesthesiologist has attended each examination.

Twenty-four examinations were carried out in these 23 patients without serious incident. (Patients with evidence of cyanosis, recent myocardial infarction, asthma or serious allergy have not been accepted for this examination.) Two patients had febrile responses, one to 104° F., within 4 hours but

TABLE I. ANGIOCARDIOGRAPHY IN DIAGNOSIS OF RESECTABILITY OF CARCINOMA OF LUNG

	MGH UNIT	INVOLVEMENT BY ANGIOCARDIOGRAPHY	PREDICTION	RESULT	OPERATIVE FINDINGS
1.	891969	1. Obstruction left pulmonary artery 2. Defect left atrium	Not resectable	Not resectable	Tumor encircling pulmonary artery and lying anterior to hilus
2.	911545	1. Superior vena cava distorted 2. Occlusion right PA, superior branch	Not resectable	Not resectable	Carcinoma involving vena cava, pulmonary artery and vein
3.	860017	1. Invasion of SVC 2. Right pulmonary artery obstructed	Not resectable	Not resectable	Extensive lymph node metastases occluding SVC
4.	661031	Upper lobe branches, left PA distorted and small	Resectable	Left pneumonect.	Tumor close to pulmonary vessels and aorta
5.	799470	Aortic arch separated from LPA by mass	Resectable	Left pneumonect.	Large tumor about LPA, adherent to aorta and pericardium; left innominate vein invaded
6.	819044	No involvement of essential vascular structures	Resectable	Right pneumonect.	Hilus free; paratracheal nodes enlarged but not by tumor
7.	923419	1. Compression of LPA near origin 2. Tumor pressing on aortic arch 3. Defect left atrium	Not resectable	Not resectable	Extensive tumor about hilus; positive prevascular nodes
8.	817615	1. Sparse filling of LPA but no occlusion	Resectable	Left pneumonect.	1/2 cm. between origin of LPA tumor adherent to outside of PA
9.	933298	Displacement and poor filling of RPA without occlusion	Resectable	Right pneumonect.	Involved lymph nodes behind UL artery; RPA ligated within pericardium
10.	811557	1. Distortion rt. innominate vein and SVC 2. First branch RPA occluded 3. Defect left atrium	Not resectable	Not resectable	Massive involvement of hilus, heart and all great vessels
11.	864448	1. Superior vena cava displaced and irregular 2. Defect left atrium	Not resectable	Not resectable	Extensive metastases about upper hilus and trachea
12.	749995	1. Pressure on inferior branches of left PA 2. Left inferior PV and left atrium involved	Not resectable	Left pneumonect.	Inferior PV invaded by tumor but removed

13.	912178	1. Obstruction of rt. innominate vein and vena cava	Not resectable	Not resectable	Extension of tumor from RUL to great vessels and trachea
14.	240628	Mass lying close to descending thoracic aorta	Resectable	Not resectable	Tumor invading aorta and posterior chest wall
15.	956094	*Left injection:* Extrinsic obstruction of lt. innominate vein, by innominate artery *Right injection:* above confirmed	Resectable	Left pneumonect.	Pulmonary involvement sufficiently distal to allow resection
16.	731983	1. Pressure on SVC minimal	Resectable	Not resectable	Extensive node metastases about upper hilus and in lt. paratracheal area; SVC pushed forward
17.	611886	1. Lt. PA occluded close to origin 2. Defect lt. atrium 3. PA separated from aorta	Not resectable	Not resectable	Massive nodal involvement of hilus and superior mediastinum
18.	152762	Poor visualization of superior branch, rt. pulmonary artery and PV	Resectable	Right pneumonect.	PA ligated within pericardium; sup. PV occluded to 1 cm. from left atrium
19.	911234	1. Narrowing of SVC 2. Occlusion first branch rt. PA	Not resectable	Not resectable	Tumor from RUL to mediastinum with pressure on SVC; extensive nodes about PA
20.	412021	Right sup. mediastinal fullness produced by tortuous rt. innominate vein and artery	Resectable	Left upper lobectomy	Small peripheral tumor in left upper lobe
21.	357396	1. Displacement and ? invasion of SVC 2. Displacement of branches of RPA	Not resectable	Not resectable	Large tumor involving RUL and mediastinum with fixation
22.	916423	1. Constriction of left PA at origin	Not resectable	Left pneumonect.	Extensive tumor with narrowest of margin of division of PA; lt. atrium invaded but segmentally removed
23.	954223	Peripheral tumor not involving vessels	Resectable	Left upper lobectomy	Primary lesion LUL; soft involved lymph nodes between PA and bronchus prevented pneumonectomy

in each instance normal temperature was present by the following morning. In another 2, urticaria appeared within an hour; in each the hives rapidly disappeared following the administration of oral Pyribenzamine. One patient noted generalized malaise for approximately 48 hours. There were no known late sequelae. In particular there was no indication of significant thrombophlebitis.

During the examination, patients experience a sense of warmth from head to toes. They become flushed and occasionally restless. There is a strong urge to cough. Within a few minutes they feel quite normal.

Fig. 1.—Tapered narrowing of the superior branch of the right pulmonary artery distal to its origin (arrow).

RESULTS OF STUDY

The following angiocardiographic evidence has been found of value in predicting unresectability.

1. Occlusion or a severe degree of narrowing of the left pulmonary artery within 1.5 cm. of its origin from the undivided pulmonary artery. Such involvement precludes separation of the branch vessel from the trunk. This corresponds with the experience of Dotter and Steinberg. Complete occlusion of the vessel usually is shown by a tapering or pointed ending seen best in the lateral projection. Certainly the length of the artery proximal to its point of involvement can be measured best in this projection or in the left anterior oblique position. Complete obstruction may be the result of other conditions and it is recognized that the finding is not direct evidence but, coexistent with pulmonary cancer, such findings are strong circumstantial evidence of malignant invasion. Narrowing of the artery in a concentric fashion also suggests, although less strongly, unresectability. Pressure upon one side of the artery,

even at a point quite close to the main pulmonary trunk, carries a much less ominous interpretation, because the tumor or a large lymph node may merely be resting against the artery and not actually invading it.

2. Occlusion or severe narrowing of the branches of the right pulmonary artery to the upper or lower lobes within 1 cm. distal to the bifurcation of the right pulmonary artery (Fig. 1). This point lies slightly more distal than considered the point of inoperability by Dotter and Steinberg. It lies just outside the pericardium. Occasionally it has been possible to ligate the right pulmonary artery more proximally by opening the pericardium.

Fig. 2.—Lateral view of superior vena cava and pulmonary artery, showing anterior displacement of the vena cava produced by lymph nodes invaded by tumor. Note nodularity.

3. Partial or complete obstruction of the innominate veins or the superior vena cava. It is quite possible to resect such structures, replacing them with venous grafts, but to date this has not been found advisable.

In addition to the overt degrees of involvement described above, very minor deformities indicative of pressure have proved significant. A tumor which presses on the superior vena cava or innominate vein may invade its wall and preclude resection, in contrast with a deformity of similar magnitude on an artery. This is particularly true if the indentation of the vein be nodular in character (Fig. 2), or if the vein be separated from normally adjacent structures (Fig. 3). It is recognized that interpreting pressure deformities as

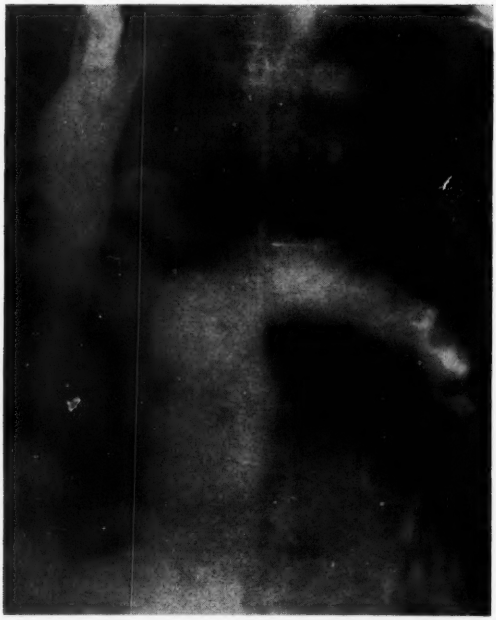

Fig. 3.—Vena cava, azygos vein, and trachea separated by enlarged azygos lymph node.

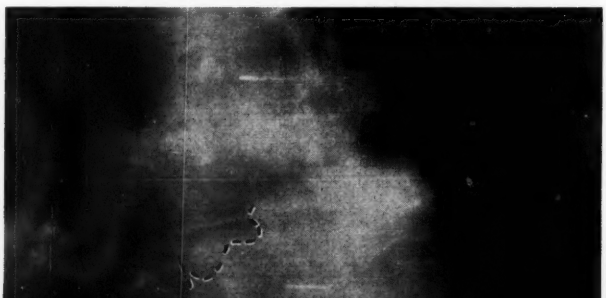

Fig. 4.—Tumor invading the right superior angle of the left atrium (dotted lines). Right superior pulmonary vein is not opacified.

caused by cancer is an assumption, but one which is usually justifiable in the presence of known primary carcinoma of the lung and in the absence of associated pulmonary sepsis, which might produce inflammatory enlargement of nodes.

4. Involvement of the major pulmonary veins or the left atrium. Normally the left atrium is smooth and regular in outline, but in 6 cases observed in this series an irregular filling defect, usually measuring 1 to 3 cm. in diameter, was visible in the heart chamber. In every instance this occurred on the same side as the primary tumor, most commonly at the superior angle near the point of entry of the superior vein (Fig. 4), but in one case at the point of entry of the inferior pulmonary vein. At times the vein adjacent to the involved atrium was also invaded. Care must be exercised in evaluating impairment or absence of visualization of a major pulmonary vein alone when the corresponding pulmonary artery is seriously embarrassed by tumor. If the artery is well outlined, however, and the vein is poorly filled with contrast material, involvement of the vein is strongly suggested, especially if there be an adjacent filling defect in the atrium.

Pericardial invasion by tumor has been recorded by Dotter and Steinberg but was not seen in our series except as a finding coincident with atrial invasion.

In our experience, preoperative prediction of impossibility of resection has been quite accurate. Thirteen cases were deemed unresectable by angiocardiography. Eleven of these were considered unresectable at thoracotomy. In two instances a pneumonectomy was performed. These patients died of residual carcinoma 6 and 7 months following pneumonectomy.

In Case 12, the left inferior pulmonary vein was seen peripherally but not proximally and there was the suggestion of invasion of the left atrium at the entrance of this vein. The removed lung showed tumor invasion of the inferior pulmonary vein.

In Case 22, the angiocardiogram showed involvement of the left pulmonary artery very close to the main pulmonary trunk. There was pressure superiorly on this common trunk. Failure to demonstrate the left superior pulmonary vein was attributed to arterial obstruction. The lung could be resected by division of the left pulmonary artery flush with the common trunk but tumor extended within 1 cm. of this margin in the resected specimen. Tumor grew along the pulmonary veins and invaded the left atrium so that a small segment of atrium had to be resected with the tumor.

It was not the primary aim of this study to predict operability. Indeed, this phase of the problem was less successfully met, but errors in this direction are considered less serious, since for the patient's sake it is much better to err in this direction than in the opposite one. Ten cases were predicted as operable by angiocardiography. Seven were confirmed at operation; 3 proved to be inoperable.

Case 14 had a tumor lying in the posterior thoracic gutter near the descending aorta. Angiocardiography proved the mass to be separate from the aorta but failed to reveal involvement of the aorta by the tumor. Exploratory thoracotomy disclosed this invasion of the aorta as well as the chest wall by the tumor.

Case 16 had a mass in the right upper lobe extending from the hilus to the chest wall. Angiocardiography showed minimal pressure on the posterior aspect of the superior vena cava below the azygos vein, but this pressure defect appeared to change and was not deemed sufficiently conclusive to warrant a diagnosis of tumor involvement. The right pulmonary artery filled slowly and seemed small but was without evidence of localized involvement. Thoracotomy disclosed the tumor adjacent to but not invading the chest wall. Lymph nodes in the mediastinum and at the right hilus were involved by tumor and pushed the superior vena cava forward without obvious invasion of this vessel.

Case 23 had a peripheral tumor in the left lung without evidence of metastasis to hilar or mediastinal nodes by conventional roentgenography or angiocardiography. Thoracotomy disclosed many grossly positive but very soft lymph nodes lying in front of the aorta, behind the pulmonary artery and between the latter and the left main bronchus. The adherence of these nodes to vessels prevented pneumonectomy.

The number of cases is obviously too small to be of any statistical importance, but the types of vascular distortion are nevertheless interesting. We have been impressed particularly by the grave significance of even minor degrees of distortion of the superior vena cava. Equally striking has been the frequency of involvement of the left atrium, which occurred nearly as often as superior vena cava deformity. These changes, which have not been stressed previously, can be appreciated only if multiple films, of good quality, are obtained, thus permitting the observer to be certain of the constancy of findings, which may be overlooked or disregarded on a single film.

SUMMARY

1. Experience with preoperative prediction of resectability of 23 cases of primary carcinoma of the lung studied by angiocardiography at the Massachusetts General Hospital is presented.

2. Thirteen cases were considered unresectable, and this was confirmed in eleven instances.

3. In 10 cases, no evidence was found which indicated involvement of heart and great vessels, and 7 were so found at operation.

4. Unnecessary thoracotomies may be avoided in cases demonstrated as unresectable by this method.

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A SIMPLIFIED METHOD FOR ACHIEVING INTRARESPIRATORY HUMIDIFICATION IN THE TRACHEOTOMIZED PATIENT

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IN THE CARE of severe respiratory conditions tracheostomy is often resorted to for varying lengths of time in order to maintain an unobstructed and patent airway in the acutely ill patient. However, the problem of intrabronchial crusts arises frequently as a complication of tracheostomy. This problem has been especially common in those patients with severe neurological diseases such as poliomyelitis, head injury, and in crush injuries of the chest.

The basic problem in the prevention of intrabronchial crusts is the prevention of inspiration of secretions by maintaining adequate tracheobronchial humidity.[1] Various methods of achieving this have been tried. One has been the direct instillation of irrigating fluids into the tracheotomy tube. These fluids are then carefully aspirated in the paralytic patient by means of semisterile technique with the realization that deep suctioning might easily traumatize the respiratory tree and cause additional mucous plug formation. The nonparalytic patient is encouraged to cough up the instilled fluids which are then suctioned out of the tracheotomy tube. The most frequently used liquids have been detergents such as Duponol-C,*[2] and Alevaire,† or isotonic saline. The use of these irrigations has resulted in a distinct decrease in mucous plug formation. The irrigations often float out the small mucous plugs before they become sufficiently enlarged to cause partial or complete obstruction of the lesser bronchial radicals. Other investigators have used herb teas, mucolytic enzymes in a suitable vehicle and drugs administered systemically in order to thin secretions.

Another method is to administer water vapor or water droplets. The warm steamer has provided more problems than solutions since constant supervision is necessary to prevent burns to the trunk, neck, and respiratory tree. Moreover, proper humidification of the tracheotomy is difficult. The cold steamer and nebulizer have proved to be more efficacious, but require fairly elaborate equipment for attachment to the tracheotomy tube. The conventional bottle bubbler attached to most oxygen-administration units provides little increase in tracheobronchial humidity. Preheating the water and

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*Duponol = C (sodium lauryl sulfate).
†Alevaire, Winthrop Laboratories.

bubbling the oxygen through additional lengths of multiholed tubing become useless unless the unit is attached within a foot of the tracheotomy tube because the change in temperature decreases the relative humidity.

Lung air contains about 6 per cent water vapor; inspired air contains about 1 per cent water vapor and oxygen, less than 1 per cent water vapor. To meet the above standard of water vapor content, a simple device was desired that could be attached to all tracheotomized patients, whether in a respirator or surrounded by other cumbersome equipment, without fear of drowning the patient and still providing adequate humidification.

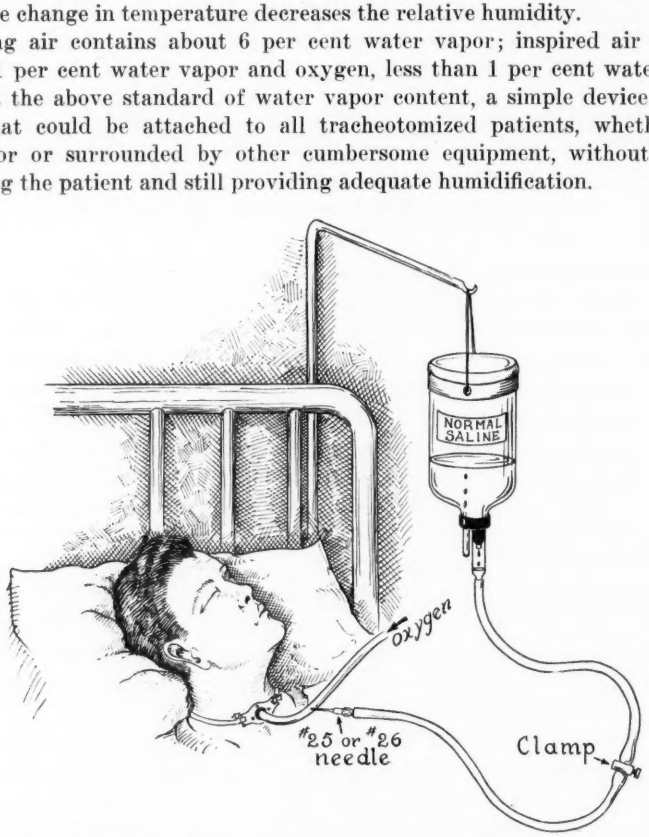

Fig. 1.—A drawing which depicts the relative simplicity of the apparatus required to achieve an adequate degree of intrabronchial humidification in the tracheotomized patient.

In experiments conducted by Basch and co-workers[3] regarding the influence of drugs and agents on tracheobronchial secretions, water vapor liquefied the secretions most efficiently. We, therefore, selected isotonic saline as the most readily available sterile solution which would satisfy the requirements of humidification.

The isotonic saline is administered by the usual intravenous tubing with a No. 25-gauge needle which is placed in the lumen of the oxygen-administration tube about 6 inches from the tracheotomy tube. The isotonic saline flow is regulated with a Hoffman clamp at 4 drops per minute. At an oxygen flow rate of 7 L. per minute the oxygen stream vaporizes the saline and disperses the larger droplets into the trachea. These droplets migrate into the respiratory tree and vaporize according to the temperature of the patient and to the

local requirements of the lung. A similar drip directly into the tracheotomy tube has been found to have the same beneficial effect of thinning the secretions even when the oxygen was not concurrently given. The isotonic saline bottle is marked "For Tracheotomy Tube Use Only" as is the regulating clamp in order to avoid confusion with the intravenous solution bottles in order to prevent accidental drowning of the patient.* Second, the bottle is kept at the level of the patient's head in order to reduce hydrostatic pressure and to prevent further the possible overly rapid administration of the isotonic saline solution.

Results over the past 4 years have shown that intrabronchial crusts definitely have been diminished. The conscious patient with a cough reflex can raise sputum with much less difficulty, thereby decreasing the endotracheal suction traumatization and ensuing complications of intrabronchial plugs, infections, and atelectasis.

SUMMARY

A simple technique is described for the maintenance of adequate tracheobronchial humidity in tracheotomized patients. This consists of a slow drip of isotonic saline through a 25-gauge needle into the lumen of an oxygen catheter. Adequate humidification is then obtained with the prevention of intrabronchial crust formation. The required equipment is readily obtainable.

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*Such an accident would be unlikely in view of the fact that, in the normal individual, up to 1 L. of physiological saline can be instilled into the lungs in a 24-hour period without ill effects.

MUCORMYCOSIS OF THE BRONCHUS SUCCESSFULLY TREATED BY LOBECTOMY

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UNTIL recently, mucormycosis infection was considered a uniformly fatal disease. Harris,[1] from this clinic, reported a diabetic patient with nasopharyngeal mucormycosis in whom the diagnosis was made during life. Recovery followed rigid control of diabetes, desensitization against the fungus, and administration of iodides.

The authors have treated a second patient in whom the diagnosis of mucormycosis was made during life. The factors which led to a satisfactory recovery of this patient form the basis for this report.

CASE REPORT

R. G. (Duke No. E30177) was a 20-year-old Negro woman who had had diabetes for at least 5 years. Two and one-half months prior to her admission to Duke Hospital she was treated at her local hospital for her first episode of diabetic coma and acidosis. A second episode, 6 weeks prior to her admission to Duke, responded well to the usual therapy for acidosis. On the sixth day of this admission she developed an elevation of temperature to 39.5° C. An area of consolidation in the right lower lung field was demonstrated by x-ray examination. In spite of penicillin therapy she did not improve and was admitted here on March 30, 1956.

On admission the temperature was 37° C., pulse 100, blood pressure 108/60 mm. Hg, and respiration 22 per minute. The trachea was shifted to the left. Over the right lower chest the breath sounds, tactile fremitus, and vocal fremitus were decreased, and there was dullness to percussion. The liver edge extended approximately 2 fingerbreadths below the costal margin and the organ was tender. The remainder of the physical examination was normal.

Laboratory studies on admission showed the hemoglobin to be 11.6 Gm., the white cell count 9,050 with 53 per cent polymorphonuclear leukocytes, 3 per cent stab forms, 2 per cent eosinophils, 10 per cent basophils, 3 per cent small lymphocytes, 22 per cent large lymphocytes, and 16 per cent monocytes. Urine examination showed a specific gravity of 1.034 and a pH of 5. There was no protein or acetone, but 4+ sugar was present. Microscopic examination of the urine was negative. *Candida albicans,* nonhemolytic *Micrococcus pyogenes* var. *aureus* and *Neisseria sicca* were grown from the sputum. Gram stain of the sputum showed a predominance of gram-negative diplococci.

A fasting blood sugar was 222 mg. per cent and serum cholesterol 266 mg. per cent.

Skin tests for old tuberculin 1:1000 was 2+ in 48 hours. Skin tests for blastomycin, coccidioidin, and histoplasmin were negative.

A chest film showed complete density of the right lower chest (Fig. 1). During the first week, her diabetes was well controlled and she began coughing up foul-smelling, purulent sputum. Fluoroscopy revealed an air-fluid level in the right lower lung field.

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Bronchoscopy on the fifth and twelfth hospital days revealed granulation tissue obstructing the distal portion of the bronchus intermedius. Bacterial culture showed aerobic Klebsiella which was strongly sensitive to Chloromycetin. No growth was obtained from cultures for acid-fast organisms and fungi. Biopsies of the area showed chronic inflammation of the wall of the bronchus. The surface was covered by a layer of necrotic tissue and fibrinopurulent exudate in which one could see many broad, irregular, nonseptate hyphae

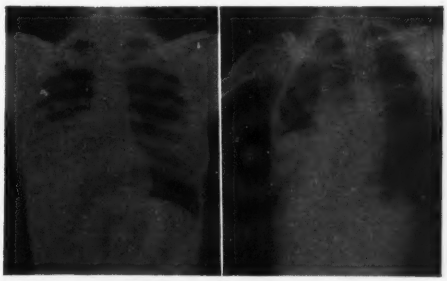

Fig. 1.—A chest film taken the day of admission shows consolidation of the right lower lung field. The air-fluid level is seen in the oblique view taken the day after admission. This persisted without change for 30 days.

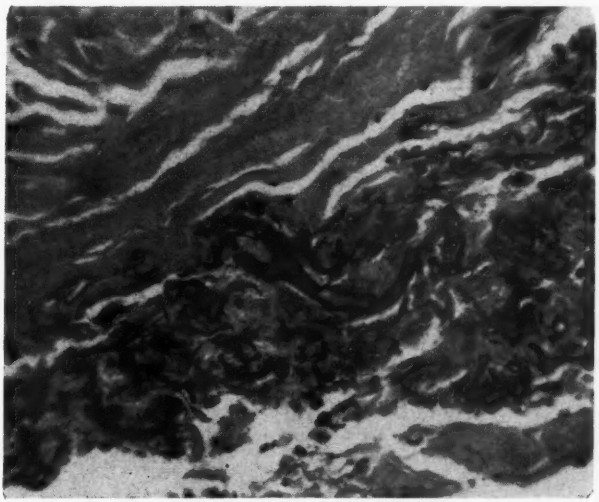

Fig. 2.—Bronchoscopy biopsy specimen. The section shows a branching, nonseptate hypha in necrotic material. (Hematoxylin and eosin; ×331; reduced ⅓.)

(Fig. 2). The fungus was almost entirely in necrotic tissue. The hyphae were basophilic and readily visible in routinely stained tissue. Bacterial stains showed numerous gram-positive cocci but no acid-fast organisms were seen.

Following the second bronchoscopy, she became worse with daily elevations in temperature ranging from 38° to 39° C. She continued about the same to the twenty-fifth hospital day, despite antibiotics, and frequently needed supplemental doses of regular insulin. Serial chest films remained essentially unchanged with the air-fluid level remaining in the right lower lung field.

On the twenty-fifth hospital day, resection was attempted but postponed because of aspiration of secretions during intubation. This cleared and on the thirtieth hospital day she was intubated under topical anesthesia with a Carlen's bronchospirometer tube and, under general anesthesia, a right middle and lower lobectomy was performed. A tracheostomy was done at the end of the procedure to maintain tracheobronchial toilet. She did well and became afebrile on the seventh postoperative day. Antibiotics were continued for 10 days after operation. Serial films following the middle and lower lobectomy on the right showed the left lung and right upper lobe to be expanded well (Fig. 3).

Fig. 3.—A chest film made 5 weeks after right middle and lower lobectomy shows good expansion of the remaining upper lobe with some postoperative pleural reaction at the right base.

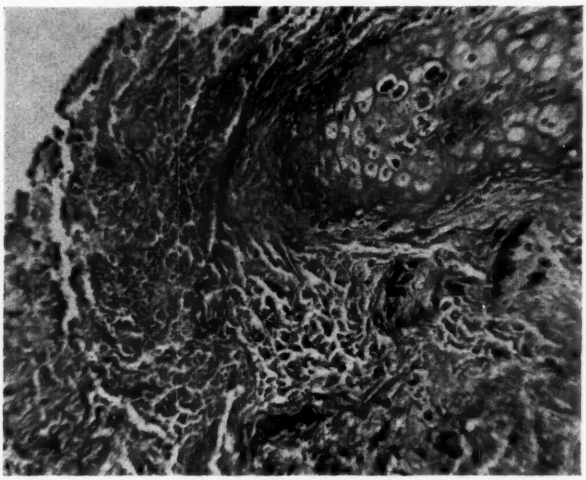

Fig. 4.—Section from bronchus of operative specimen. The section from the wall of the bronchus intermedius shows hyphae extending deep to the bronchial cartilage. (Hematoxylin and eosin; ×167; reduced ⅙.)

Gross examination of the lobes removed showed a large abscess containing 30 to 40 c.c. of sanguino-purulent material in the lower lobe, with atelectasis and consolidation of the middle lobe. Sections taken from the superior segment of the lower lobe, basilar portion of the lower lobe, through the parenchyma of the middle lobe, and from the wall of the abscess of the lower lobe showed only chronic nonspecific pneumonia with abscess formation.

Sections through the bronchus intermedius and adjacent lymph nodes showed marked necrosis of the bronchus with infiltration of the bronchus by nonseptate hyphae (Figs. 4 and 5).

She was discharged on the forty-third postoperative day. The diabetes was controlled on a 2,100 caloric diet with 52 units of NPH insulin with 5 units of regular insulin administered in the morning. A vaccine made up of *Candida albicans* and Mucor, 1:1000 dilution, had been started while in the hospital to be continued three times a week by her county health office.

Although she has not returned here for follow-up, a report from her county health office states she continued to do well for 6 months following discharge and then moved out of the state.

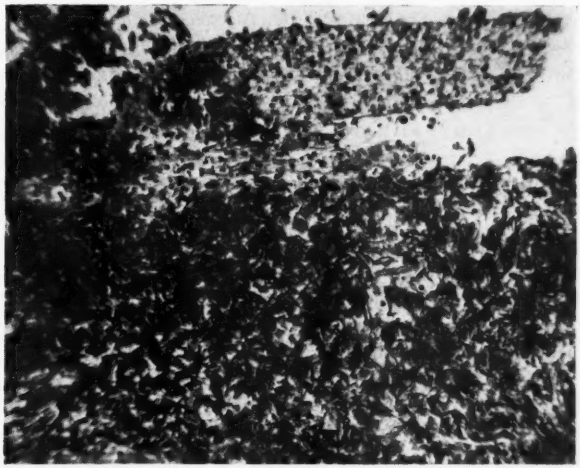

Fig. 5.—Section from bronchus of operative specimen. The section shows a matted mass of hyphae lying on the epithelial surface of the bronchial wall. (Hematoxylin and eosin; ×167; reduced ⅕.)

DISCUSSION

Pulmonary mucormycosis has been reviewed recently by Baker.[2, 3] In his series of patients, all of whom died, the disease occurred only in those who had concomitant disease that could have reduced the resistance of the body to infection. Diabetes mellitus, multiple myeloma, leukemia, infant diarrhea, and thermal burns were among the predisposing factors.

This is the first reported patient who has had a pulmonary resection for mucormycosis and the second patient in whom a diagnosis has been made during life. From similar patients, previously reported, it is apparent that a pre-existing severe illness is necessary for the establishment of pulmonary mucormycosis. In our patient, diabetes mellitus with acidosis and coma was the predisposing factor in reducing resistance to infection. With the marked inflammatory reaction and destruction of the bronchial wall, obstruction was produced. This then favored the development of a bacterial abscess distally.

The principal factor necessary to effect a cure of a patient with mucormycosis is to control the pre-existing disease as advocated by Harris.[1] Removal of the nonareated destroyed lung in our patient was a second essential factor,

for this removed an area that harbored an infection and made control of the diabetes possible. Invasion of blood vessels of the lung by the Mucor with resultant infarction, as so frequently occurs, was not found in our patient. The limitation of fungus infection to the bronchus, followed by normal healing of the bronchial stump was, we felt, due to the rigid control of her diabetes.

The fungus was not grown from this patient possibly because the number of fungi were few as compared to the number of other organisms. The fungus in the tissue was confined to a small segment of the bronchus and was not seen in the cavity in the lung. The cavity distal to the site of fungus infection was a typical pyogenic abscess such as one usually sees with bronchial obstruction. The fungus could not be identified in the wall nor could one see the usual reaction associated with the presence of this fungus, namely, necrosis of tissue with little or no cellular infiltrate. The organism would surely have grown if a portion of the bronchus had been used as inoculum. Phycomycetes are readily recognized in tissue sections by the masses of nonseptate hyphae and, when invasive into the tissue, may be considered pathogenic.

SUMMARY

This is the first case of pulmonary mucormycosis in which a pulmonary resection was performed, and the second case in which the diagnosis was made during life.

The pathogenesis and course is discussed.

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ACCESSORY LUNG WITH PERSISTENT LEFT SUPERIOR VENA CAVA AND DUPLICATION OF INTESTINE

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IN comparison with other malformations of the lung, accessory lung is an uncommon observation. Herxheimer,[1] in 1901, described a normally aerated accessory lung. He found a small functional "third lung" stemming from a tracheal bronchus 2.5 cm. down from the cricoid cartilage. This accessory lung "set above the lung on the right side" had caused stenosis of the trachea when it pressed against the right side of this structure. However, he did not describe the origin of the blood supply to this accessory lung. The second case of true accessory lung was reported by Müller.[2] This, like that of Herxheimer, was a right-sided accessory lung originating from the trachea. Again details of blood supply are absent even though he describes an artery and a vein to the accessory lung on serial microscopic sections. Tracheal diverticula and tracheal accessory lungs were discussed many years ago by Chiari.[6] In 1940, Hulse and Curtis[3] reported a case of a true tracheal accessory lung which was diagnosed by bronchogram. Cotton, Spaulding, and Penido[4] reported a whole true accessory lung with three lobes located in the right thorax. This was said to be the first instance of a true accessory lung removed by surgery. The blood supply was a single branch of the subclavian artery. The upper, accessory cystic lung came directly off the trachea by a stem bronchus that measured approximately 3 mm. in diameter and 1 cm. in length. In 1953, Seley[5] reported what he said to be the first recorded instance of an accessory lung situated in the suprahilar area receiving an artery from the aorta and showing evidence of cystic disease and sequestration.

The purpose of this report is to define and discuss a case of pure or true accessory lung. This malformation is to be clearly delineated from other conditions with which it is confused. Loosely defined terms such as ectopic, supernumerary, aberrant, lower accessory lobes, tracheal diverticula, bronchogenic cysts, etc., have confused the issue of the exact morphology of true accessory lung. The case presented in this report afforded an opportunity to inject the arterial and venous blood supply to the accessory lung and thereby trace the exact origin and course of these vessels.

CASE REPORT

A one-month-old white female child was admitted to the Medical College of Virginia Hospital on June 5, 1956, because of chronic constipation, straining at stool and the recent

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appearance of a mass at the anus. The infant was born one month prematurely and weighed 5 pounds and 6 ounces at birth. From the beginning, the infant ate an evaporated milk formula poorly and spit up a good deal of each feeding. The stools had always been small, hard, and yellow. Approximately one week prior to admission the infant began to strain more during defecation and at this time the mother noted a mass at the anal orifice. On the day before admission, she noted some bright red blood on the diaper. There had been no vomiting, fever, or other symptoms and the history was otherwise negative.

Physical Examination:—Temperature 98.6° F., weight 5 pounds, 13½ ounces, pulse 150, respiration 30. The general appearance and the physical examination were not abnormal except for the findings confined to the anus and rectum. On straining there appeared to be protrusion of the rectal mucosa on the left side of the anus and laxity of the perineum. Digital examination revealed a tubular cystic mass encroaching on the left side of the anus, rectum

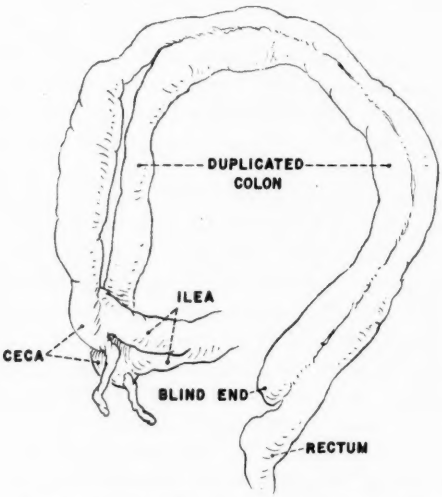

Fig. 1.—Duplicated small and large intestines.

and rectosigmoid. The mass was between the rectum and pelvis. There did not appear to be any connection between the mass and the sacral and retroperitoneal region posteriorly, nor did there appear to be any connection by a stalk between the mass and the rectal mucosa higher up. The examining finger could not be inserted between the mass and the external circumference of the anus. The lumen of the anus and rectum appeared adequate for bowel movement.

Laboratory Data:—The urinalysis was negative. Hemoglobin 15.2 Gm.; white blood cells 17,800 with 42 per cent polymorphonuclears, 1 per cent eosinophils, 25 per cent lymphocytes and 32 per cent monocytes. Smear showed a strong shift to the band stage and severe toxic changes. Serum sodium 145, potassium 6.0 mEq./L., chlorides 97 mEq./L., and CO_2 22 mEq./L., respectively. BUN was 17 mg. per cent.

A barium enema on the day after admission revealed a very redundant but normal-sized colon with questionable malrotation of the cecum. Filling was not completely satisfactory. Evacuation was poor. Roentgenograms of the chest revealed a normal cardiac shadow with slight prominence of the bronchovascular markings throughout and linear densities in the right upper lung "compatible with linear atelectasis or residual changes of pneumonia." A gastrointestinal study with Lipiodol was also negative.

Following admission, the infant was placed on a Similac formula. She took feedings fairly well for the most part with variable amount of regurgitation. The weight had increased to 6 pounds, 4 ounces by the sixteenth hospital day when a laparotomy was performed.

Operative Findings:—On inspection of the peritoneal cavity, it was apparent that the terminal ileum was duplicated as well as the cecum and the appendix. There was a duplicated large intestine down to and below the peritoneal reflection (Fig. 1). The duplicated colon had a mesentery of its own from the terminal ileum up to the mid-transverse colon. At this point the wall became common with the normal colon. The duplicated colon was three times normal size, cystic in nature and its walls were definitely thickened. The duplicated terminal ileum was resected and the proximal line closed with silk sutures. The duplicated cecum, appendix ascending colon and proximal transverse colon which had its own mesentery was resected without difficulty and the distal orifice of the duplicated colon was exteriorized as a fistula.

Fig. 2.—The two lobes of the left lung are reflected forward, revealing an aerated accessory lung lying in the posterior part of the thoracic cage and separated from the left lung by a translucent sheet of pleura.

Postoperatively, the infant did satisfactorily until the eighth postoperative day when she developed vomiting and subnormal temperature. The respiration became difficult and there was marked inspiratory retraction with greenish mucoid material exuding from the nose. There was intense cyanosis and coarse rhonchi and râles throughout the chest. The patient died.

Autopsy Findings.—There was an accessory lung lying in the posterior portion of the left upper part of the pleural sac (Fig. 2). This lung possessed its own pleural cavity and like the other lobes of the lungs was well aerated. This latter finding accounted for the fact that no mass or lesion was seen by x-ray. The accessory lung had a communication with the trachea by an eparterial bronchus which arose from the left side of the trachea less than 1 cm. above its bifurcation. The lungs with their six lobes and their contained blood supply were injected with vinylite plastic (Fig. 3). The result of this showed that the accessory lung was supplied on the arterial side by a branch of the left main pulmonary artery. The venous return was by the pulmonary veins. An additional anomaly was drainage of the azygos system into a left persistent superior vena cava (duct of Cuvier) which drained into the left atrium.

Anatomic Diagnosis.—Duplication of the terminal 2 cm. of ileum, cecum, appendix, ascending colon, transverse colon, descending colon, sigmoid colon, and upper rectum.

Surgical resection of duplicated terminal ileum, appendix, cecum, ascending colon, and proximal transverse colon.

Localized fibrinous peritonitis of colostomy site.

Colostomy, anterior abdominal wall, involving proximal end of duplicated large bowel not surgically removed.

Duplication of left lung—accessory left lung with its own pleural cavity.

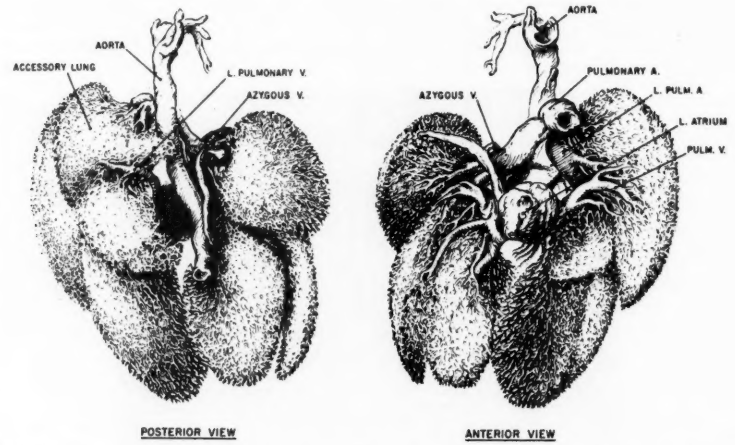

Fig. 3.—The vinylite plastic injection according to the method of Liebow. The accessory lung is supplied by a pulmonary artery and drained by a pulmonary vein. There is no connection with the aorta.

DISCUSSION

There appears to be little or no difficulty in defining the anatomic features of such pulmonary anomalies as azygos lobes, bronchogenic cysts, congenital cystic disease, mediastinal cysts, and tracheal diverticulum. Review of the literature quickly demonstrates the confusion between terms such as true accessory lung, pulmonary sequestration and pulmonary sequestration of accessory lobes and, finally, aberrant and heterotopic lung. In our opinion, true accessory lung is composed of two or more lobes, is contained in its own pleura, and derives a bronchus from either the trachea or the main-stem bronchus.

Furthermore, both the arterial and venous blood supplies are entirely pulmonary in derivation and course. In other words there is no supply from the systemic arteries. The aberrant lobes have no connection with the trachea or bronchi and the blood supply is from the systemic artery. Pulmonary sequestration is a malformation characterized by "cutting off" of the developing lung and, as would be expected, possesses a systemic blood supply. From a review of the literature and our own case we are of the opinion that the development of a true accessory lobe is *not* brought about by the mechanism of pulmonary sequestration. It is more accurately a duplication or supernumerary process. It is our feeling that the case presented in this report supports our view in that

it showed not only duplication of the lungs, but also intestinal duplication. The anomalous or persistent venous return to the left atrium and the left persistent vena cava are of passing interest in this case.

SUMMARY

A case of true accessory lung, duplication of intestines, and anomalous venous return to the left side of the heart is reported. It seems probable that the accessory lung should be so designated only if the following criteria are fulfilled: origin from the trachea or main-stem bronchus, a pulmonary blood supply, and a separate pleural cavity.

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THREE PRIMARY CARCINOMAS OF THE LUNG ARISING IN A LEFT LOWER LOBE WITH METASTASIS OF TWO OF THE TUMORS

A Case Report

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INTRODUCTION

THE following case exhibited 2 primary tumors, composed of 3 histologically different variants of bronchogenic carcinoma, all arising in the lower lobe of the left lung. These variants were a well-differentiated squamous carcinoma forming keratin "pearls," a well-differentiated papillary adenocarcinoma, and an undifferenitated (oat cell) carcinoma. The latter 2 neoplasms produced metastases in regional lymph nodes and distant organs of "pure strains" or "lines" of tumor with no admixture or intermingling of the oat cell and adenocarcinoma in any of the metastases. There was no metastasis from the well-differentiated squamous carcinoma.

The case touches on continuing problems in clinicopathologic correlation and affords yet another example of unnecessary delay in a patient having clear indications for surgical intervention. When operation was permitted in this patient with significant cardiac disease, expert anesthesia and careful attention to detail permitted thoracotomy and lobectomy to be completed uneventfully.

CASE REPORT

A 62-year-old white man was admitted to The George Washington University Hospital for investigation of a lesion of the left lung noted on a roentgenogram. The patient had had a cough for 4 years attributed to chronic bronchitis. He had arteriosclerotic heart disease with several episodes of congestive failure controlled by digitalis, diuretics, and low sodium intake. He had recently been studied because of albuminuria, casts and hematuria, and a presumptive diagnosis of right renal vein thrombosis had been made.

Roentgen examination at another institution showed a shadow in the left lower lung field. He was advised by a physician to have nothing done about it because of his cardiac status. Six months later, the patient had some pain in the left chest area. Increase in the size of the lesion in the left lung could be seen in a second roentgenogram (Fig. 1), and surgical consultation was sought. Thoracotomy was advised despite the patient's heart disease since the pulmonary shadow was thought to be a tumor and there was no clinical evidence of distant metastasis.

Physical examination revealed a well-developed, well-nourished, white man. Blood pressure was 200/100 mm. Hg. Rhonchi were heard in the left chest below the scapula. The heart was enlarged to the left and auricular fibrillation was present.

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Laboratory studies showed albuminuria and a blood urea nitrogen of 27 mg. per cent; hemoglobin 13.1 Gm. per cent; hematocrit 45 per cent; white cells, 6,650, with a normal differential; microscopic examination of the urine was negative.

A left thoracotomy was performed under Pentothal-nitrous oxide-ether-oxygen, endotracheal anesthesia. During anesthesia there was a fall in blood pressure which was controlled by a vasopressor given in continuous intravenous drip.

Palpation of the left lung at operation disclosed 2 distinctly separate masses in the left lower lobe. The first mass lay in the superior segment of the left lower lobe, was ovoid and firm, and was adjacent to the interlobar fissure. The second mass occupied the lateral basal segment of the left lower lobe. Large hard lymph nodes were present at the hilum

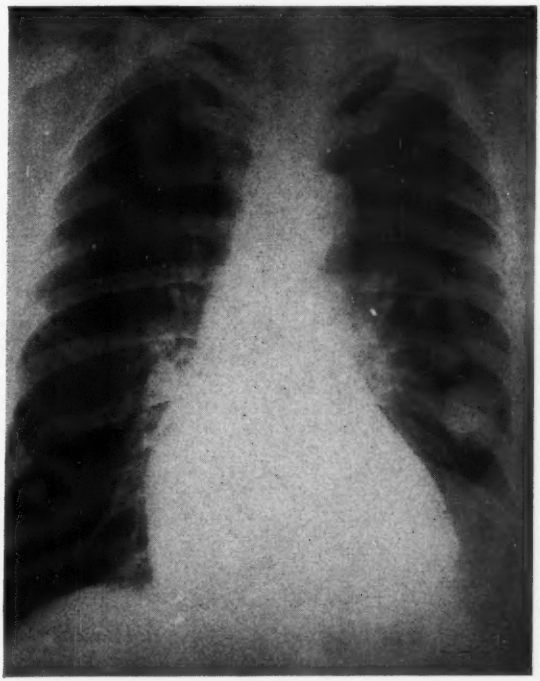
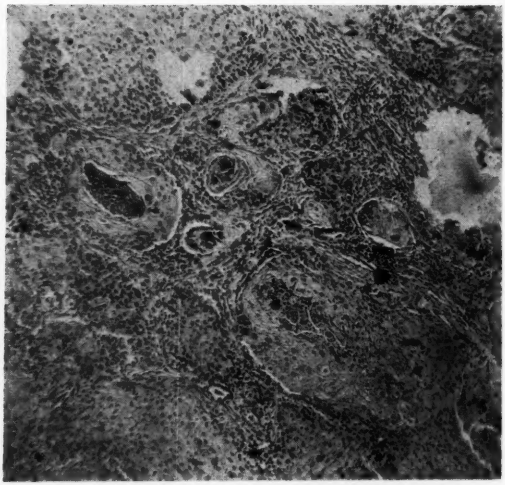


Fig. 1.—Roentgenogram of chest just prior to thoracotomy.

and in the inferior pulmonary ligament. Biopsy and frozen section of the mass in the superior segment was reported as epidermoid carcinoma. Because of the patient's cardiac status, pneumonectomy was deemed inadvisable. Left lower lobe lobectomy and hilar lymphadenectomy were performed. There was no cardiac or respiratory embarrassment postoperatively. The wound healed per primam, and he was discharged on the ninth postoperative day.

Operative Specimen.—The specimen consisted of the lower lobe of a left lung and measured 12 by 21 by 6 cm. The bronchus to the lateral basal segment contained inspissated mucus and could be traced into a circumscribed, nonencapsulated, ovoid, gray-white tumor with focal areas of necrosis. It measured approximately 4.0 cm. in diameter. The bronchus to the superior segment of the left lower lobe was the site of origin of another circumscribed, nonencapsulated, gray-white tumor measuring approximately 3.5 cm. The 2 masses were discrete and separated by an area of uninvolved parenchyma. Several hilar lymph nodes and a specimen labeled "node from lingula" were also received.



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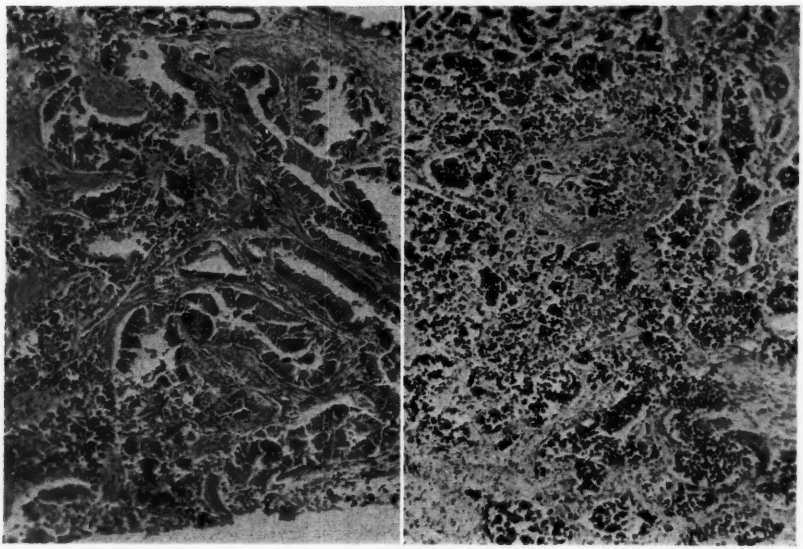


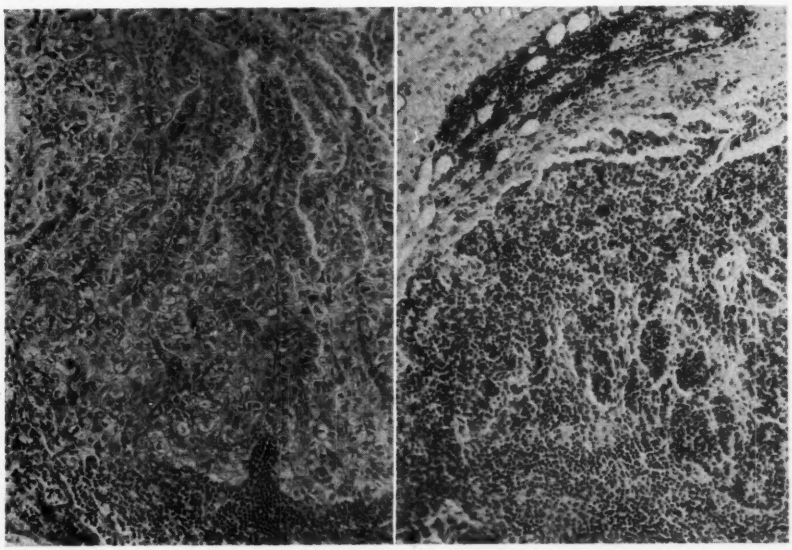
B. *C.*

Fig. 2.—*A*, Well-differentiated squamous carcinoma forming keratin "pearls" from superior segment of the left lower lobe. (Hematoxylin and eosin; ×100; reduced ⅕.)

B, Zone of admixture of well-differentiated adenoearcinoma and anaplastic (oat cell) carcinoma in lateral basal segment. (Hematoxylin and eosin; ×120; reduced ⅕.)

C, Oat cell carcinoma, lateral basal segment, showing vascular invasion and obliterative endarteritis. (Hematoxylin and eosin; ×120; reduced ⅕.)

On microscopic examination, the tumor from the upper lesion (superior segment) was a well-differentiated squamous carcinoma with "pearl" formation (Fig. 2, *A*). Its bronchial origin was seen microscopically and extensive areas of in situ carcinoma were noted adjacent to the infiltrating component. The lower mass (lateral basal segment) was composed of 2 distinct types of tumor: a peripheral portion, consisting of a papillary adenocarcinoma of bronchiolar origin (Fig. 2, *B*), and a proximal component showing an undifferentiated anaplastic carcinoma compounded of small ovoid to pyriform cells measuring 10 to 16 mμ with scanty cytoplasm (oat cell carcinoma) (Fig. 2, *C*). There was extensive vascular and lymphatic invasion by tumor with obliterative endarteritis and thrombosis (Fig. 2, *C*). There was a mingling of both elements at the mid-portion of the lesion (Fig. 2, *B*), but relatively "pure" types proximally and peripherally. No zones of transition were found.



A. *B.*

Fig. 3.—*A*, Lymph node, left hilum, containing metastatic adenocarcinoma. (Hematoxylin and eosin; ×120; reduced ⅕.)

B, Lymph node, left hilum, replaced in part by metastatic anaplastic carcinoma (oat cell). (Hematoxylin and eosin; ×120; reduced ⅕.)

Each of the elements had metastasized separately to hilar lymph nodes, some of the nodes containing metastatic papillary adenocarcinoma (Fig. 3, *A*), while others were in part or completely replaced by the "oat cell" element (Fig. 3, *B*). There was no intermingling or juxtaposition of cell types in any of the nodes. The well-differentiated squamous carcinoma with keratin "pearls" from the superior segment was not found in any of the lymph nodes.

Subsequent Course.—Three months after operation, the patient slipped and injured his left hip. He was re-admitted to The George Washington University Hospital where x-ray examination showed a pathologic fracture of the neck of the left femur. Metastatic lesions were also found by x-ray studies in the ribs, left scapula, and right clavicle. The liver was noted to be enlarged and it was evident that the patient had lost considerable weight. Internal fixation of the neck of the left femur was performed under general anesthesia. Postoperatively, the patient became more feeble and was disoriented. He was discharged 3 weeks after this admission at the request of his family. He was admitted to another hospital one week after his discharge from The George Washington University Hospital and died on the following day.

(We are indebted to Colonel J. E. Ash, M.D., pathologist, Suburban Hospital, Bethesda, Md., for a copy of his post-mortem findings and slides and permission to quote from his protocol.)

Summary of Pertinent Findings at Post-mortem Examination.—

No free fluid in thoracic or abdominal cavities.

Heart. 530 grams: Atheromatosis of aortic valve. Moderate degree of coronary sclerosis most marked in the circumflex branch of the left coronary artery. Area of scarring at apex of left ventricle suggesting old infarction. The interventricular septum contained a solitary metastatic nodule measuring 0.8 cm.

Lungs. Right 610 grams, left 530 grams: Right lung voluminous due to emphysema of the upper and middle lobes. Some collapse of the lower lobe with small nodules of metastatic tumor and a calcified tubercle. Hilar lymph nodes on the right enlarged and replaced by tumor. The remaining left upper lobe was firmly adherent to the parietal pleura and showed fibrous pleuritis. Many nodules of tumor were seen in the left hilar region.

Liver. 1,730 grams: Many umbilicated nodules of metastatic carcinoma, more pronounced in the right lobe.

Gall bladder: Metastatic tumor nodules in the wall of the fundus. Large tumor-bearing node related to the cystic duct, with no obstruction to biliary drainage.

Pancreas: The pancreas was the site of a tumor measuring 8 by 5 cm. which almost entirely replaced the body and tail of that organ and extended into the surrounding tissues with involvement of peripancreatic and coeliac nodes.

Kidneys. Right 180 grams, left 140 grams: Each contained multiple metastatic nodules in their cortices varying from 0.5 to 1.5 cm. The right renal vein was normal.

Gastrointestinal tract: Recent ulcer of the lesser curvature 1.5 cm. in diameter.

Great vessels: Moderate atherosclerosis of abdominal portion of the aorta. Metastases in para-aortic and retroperitoneal nodes.

Microscopic Examination.—

The separate "lines" of metastasis from the lower tumor found in the hilar lymph nodes at the time of the operation were still evident in autopsy sections of regional nodes and distant organs.

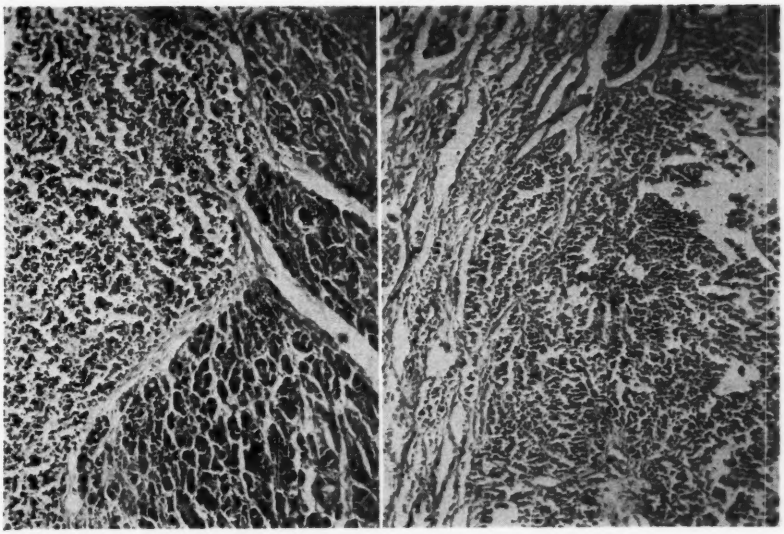
The bulk of the metastases were those of the "oat cell" component and were found in the pancreas (Fig. 4, *A*), kidneys (Fig. 4, *B*), periadrenal tissues, heart, gall bladder wall, and lymph nodes.

The papillary adenocarcinoma (bronchiolar component) was found in the right lower lobe (Fig. 4, *C*), right hilar lymph nodes and kidneys (Fig. 4, *D*).

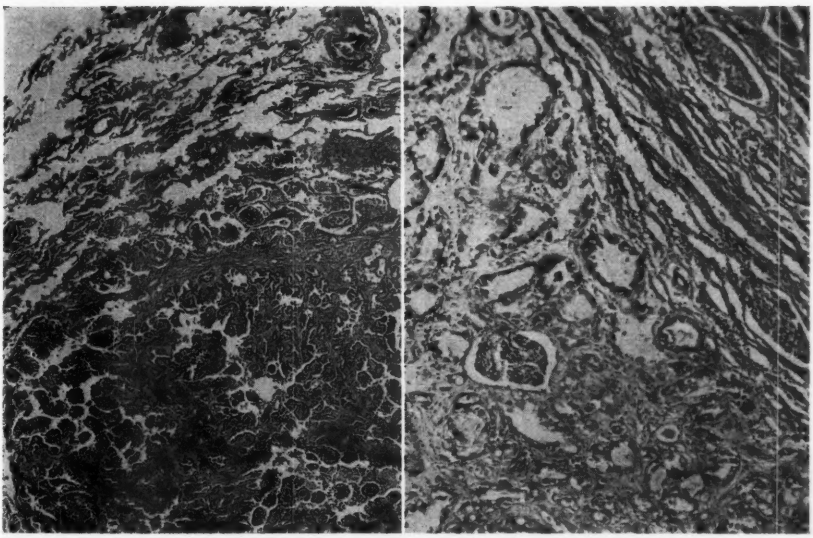
There was no intermingling or admixture of the 2 components in lymph nodes or kidneys, each element, remaining separate in each of the metastases. Reticulum stains showed a moderate amount of stromal reticulin but none was produced by the tumor cells. Mucicarmine stains showed mucin in the (often papillary) adenocarcinomatous component, but none in the "oat cell" portion. There was no metastasis from the well-differentiated, keratin producing, squamous carcinoma of the superior segment of the left lower lobe (see Fig. 2, *A*) found in the lobectomy specimen. No section of liver was available for microscopic examination.

DISCUSSION

This case is unique in our experience by virtue of the "pure strains" or "lines" of tumor, with no zones of transition, found in the primary sites in the left lower lobe and maintained in regional node and distant organ metastases. It would appear to fit in the classification devised by Foulds as a rare instance of "independent primary tumors."[1] Some recent papers with photomicrographs



A. *B.*



C. *D.*

Fig. 4.—*A*, Pancreas with metastatic oat cell carcinoma. Hematoxylin and eosin; ×90.) *B*, Kidney with metastatic oat cell carcinoma. (Hematoxylin and eosin; ×90.) *C*, Metastatic adenocarcinoma, right lower lobe lung. (Hematoxylin and eosin; ×30.) *D*, Kidney with metastatic adenocarcinoma. (Hematoxylin and eosin; ×90.) (All photomicrographs reduced ⅕.)

showing juxtaposed histologic variants of bronchogenic carcinoma do not indicate whether each element metastasized separately[2, 3] as occurred in the present instance.

It touches, too, in microcosm, on many points found in some recent papers dealing with carcinoma of the lung including the re-emphasis on classification based on histology,[4, 5, 6] site of origin of pulmonary cancer correlated with histologic type,[7] the significance[4, 6-13] or lack of significance[5, 14, 15] of cell type, and the location of metastases compared with cell type.[16] In two excellent recent papers, Walter and Pryce[4, 7] have correlated the histologic type of pulmonary cancer with the site of origin in a large series of surgically resected and necropsy specimens. Their observations with regard to data gleaned from surgical rather than necropsy material are important, as is their insistence, along with Willis, on greater recognition of the secondary changes in tumors which obscure cell type and make comparisons of different authors' classifications difficult. These two papers[4, 7] are of particular value in helping to establish that disparate statements in the literature may be due to the use of necropsy material alone[5, 15] rather than surgical specimens used in concert with necropsy findings. For example, few people would agree with Olcott's impression of the clinical course and behavior of oat cell carcinomas of the lung derived from his 8 cases.[5] The general experience with oat cell carcinoma (also evidenced here by the extent of the metastases of this component) conforms fairly closely to the reports from the Mayo Clinic.[9] Survival beyond one year after surgical resection is a rare occurrence. It may be that patients in whom a diagnosis of oat cell carcinoma can be made by bronchoscopic biopsy should have no further operative intervention as implied by the findings from the Mayo Clinic.[9]

In recent years, renewed emphasis has been placed on the correlation of cell type with clinical course[7, 8-13, 17] although some have denied that it has any role in helping to determine prognosis and survival.[3, 14] It is becoming increasingly evident that there are many interrelated and interdependent factors (rather than any single one) which are important in improving operability, survival, and salvage rate for carcinoma of the lung. Among these factors (not only in carcinoma of the lung but at other sites as well) are histologic type, location and size of the primary tumor, presence or absence of vascular and lymphatic invasion, and the status of the margins of resection as well as a group of only dimly envisioned "host factors" (See Ref. 18).

Yet another facet of this case, apart from the presence of the 3 distinct primary carcinomas with separate lines of metastasis of 2 of the tumors, is the problem of multicentric versus unicentric origin of carcinoma of the lung. McGrath, Gall, and Kessler[2] used the variations in histologic type found when preparing large tissue sections of pulmonary tumors as one basis for support of the theory of the multicentric origin of bronchogenic carcinoma, but apparently none of their "mixed" cases metastasized as distinctive histologic entities. The striking illustrations by these same authors[2] of in situ carcinoma in bronchi adjacent to infiltrating tumor as well as multiple sites in bronchi well

away from zones of infiltration would seem to leave little doubt as to multicentric origin. This would appear to us to be a more useful basis on which to support the theory of multicentric origin of carcinoma of the lung than the variation in cell type. In the present case, extensive areas of in situ carcinoma were found in the bronchus of origin adjacent to the infiltrating portion of the well-differentiated squamous carcinoma in the superior segment of the left lower lobe.

Areas of in situ oat cell carcinoma and bronchiolar adenocarcinoma were also recognized away from areas of infiltration. The microscopic appearance of the tumors at these sites was reminiscent of some of the photomicrographs published in recent papers by Spain and Parsonnet[19] and Horrell and Howe[20] both of which lend strong support to the concept of the multicentric origins of carcinoma of the lung.

There seems to be a wider acceptance of this concept when applied to terminal bronchiolar adenocarcinoma than to the squamous and oat cell variants and, for this point, the large section mounts of McGrath, Gall and Kessler[2] offer strong additional evidence that all variants of bronchogenic carcinoma are multicentric in origin, as does the paper by Papanicolau and Koprowska.[21]

An impressive array of data supporting the concept of multicentric origin at many different sites in the body has been gathered and added to personally by Willis,[15] Stewart,[18] Slaughter[22, 23] and Collins and Gall.[24]

The clinical implications of the theory of the multicentric origin of cancer are manifold. Particularly pertinent to present-day modes of therapy are the margins in excisional surgery,[2] "recurrence" of carcinoma versus new primary tumors[22, 23] and the paramount need for more frequent examination and closer observation of that particular organ or system in which patients have developed their initial primary cancer.

SUMMARY

A case report of 3 primary bronchogenic carcinomas arising in a left lower lobe is presented. Two of these neoplasms metastasized separately to regional nodes and distant organs. Problems of clinicopathologic interest and the theory of the multicentric origin of cancer evoked by the case are discussed briefly.

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EXPERIMENTAL PREVENTION OF VENTRICULAR FIBRILLATION FOLLOWING HYPOTHERMIA AND INDUCED CARDIAC ARREST

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GREAT progress has been made in the field of intracardiac surgery in the past few years. Among the factors making this possible has been the use of hypothermia to protect the cardiac and cerebral cells during periods of cessation of circulation.

Hypothermia, however, has certain inherent dangers which complicate its general application. The greatest of these is the increased susceptibility of the hypothermic heart to ventricular fibrillation. Several factors are prominent in this increased susceptibility to fibrillation and steps to prevent these are essential. It has been well shown that one of the greatest factors in the production of fibrillation is that of hypoventilation and a subsequent fall in the pH of the blood.[1, 15] It is also known that the potassium level falls consistently while the calcium level rises with a fall in the temperature.[3] Sodium and magnesium levels apparently remain constant.[2]

Hooker,[6] in 1930, showed that potassium chloride was effective in the treatment of ventricular fibrillation. However, Kyle and Kirby[9] have recently shown that potassium chloride is not as effective as electric shock, notwithstanding earlier reports that electric shock was ineffective during hypothermia.[15] They point out that a serious disadvantage to the use of potassium chloride is that cardiac arrest occurs in diastole as the result of myocardial depression and there is then difficulty in establishing a normal rhythm.

Although defibrillation can be accomplished by the use of potassium chloride or by electric shock, the prevention of ventricular fibrillation is the desired goal. Magnesium sulfate, quinidine, and the antihistamines were studied pursuant to this objective.

Magnesium has long been known to be a myocardial depressant through its action on delay of the A-V and ventricular conduction times[12, 13, 14] and, in sufficient concentration, is known to cause cardiac standstill.[11] Quinidine also, is a myocardial depressant affecting general myocardial excitability as well as conduction and contractility. Its action has been studied in normothermic animals and it has been shown that 10 mg. per kilogram given intravenously will protect the myocardium from ventricular fibrillation induced by

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an electric shock, although fibrillation can still be produced by a stronger current or repeated shocks.[4, 7, 8, 10] Antihistamines have been shown to have an effect similar to quinidine in normothermic animals.[8]

EXPERIMENTAL WORK

Method.—Adult mongrel dogs were anesthetized with sodium pentobarbital (30 mg./Kg.) and cooled in an ice and water bath to a rectal temperature of 31° C. In all cases, the temperature would then fall to 27°-29° C. during the operation. After intubation and mechanical respiration, both chest cavities were opened through the fourth intercostal space and the sternum transected. The azygos vein was ligated and the superior and inferior venae cavae dissected and umbilical tapes passed around them. After opening the pericardial sac, the base of the aorta was dissected free and a tape passed around it. A tape was also passed through the transverse pericardial sinus for identification. (In later cases, we found that the operation could be done as easily through the right chest alone and that the animals tolerated the procedure much better when the sternum was left intact.)

After occlusion of the venae cavae for 45 seconds to allow the heart to empty, the aorta was occluded and various cardioplegic mixtures in 8 c.c. volume were injected proximal to the aortic occlusion and distal to the aortic valve cusps to ensure perfusion of the coronary arteries. A Berman* vascular clamp (Fig. 1) was then placed across the aorta and pulmonary artery through the transverse pericardial sinus. This not only prevents the backflow of the cardioplegic mixture from the coronary system, but prevents the possibility of coronary air embolism in cases of septal defects wherein the approach is through the right heart.

The experimental studies were divided into 4 groups according to the cardioplegic material used. The figures summarizing each of these groups express, under "Results," what occurred after the 5- to 7-minute period of induced cardiac arrest.

Acetylcholine: In the first group (Table I), 100 mg. of acetylcholine in 8 c.c. volume was perfused into the coronary system with standstill of the heart

TABLE I. ACETYLCHOLINE*

ANIMAL	RESULT
I	Ventricular fibrillation
II	Ventricular fibrillation
III	Ventricular fibrillation
IV	Ventricular fibrillation
V	Normal rhythm followed by ventricular fibrillation
VI	Ventricular fibrillation
VII	Ventricular fibrillation
VIII	Normal rhythm
IX	Ventricular fibrillation after 7 minutes of weak contractions

*In each case the procedure was carried out at a temperature of 28°–29° C. Acetylcholine, 100 mg. in 8 c.c. volume, was perfused through the coronary system to produce cardiac arrest.

*Jacob K. Berman, M.D.

occurring immediately. During the period of occlusion of 6 to 7 minutes, the heart in all cases would gradually resume a slow bradycardia. During this period of occlusion the septum was explored through a right auricular incision. In 6 of the 9 animals, ventricular fibrillation occurred with the return of inflow of blood or when cardiac massage was used in an attempt to restore normal rhythm.

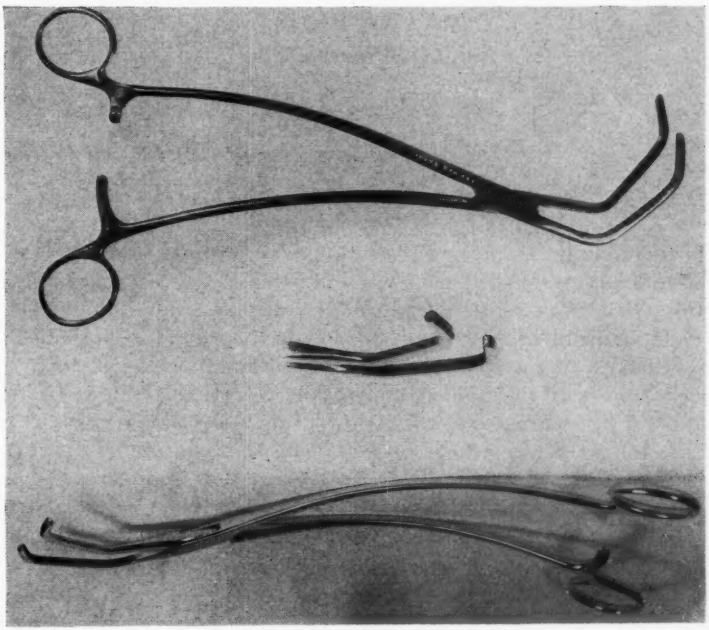

Fig. 1.—The All-Purpose Vascular Clamp. The clamp is useful in those situations where compression by a vertical device is more desirable than occlusion by the various horizontal hemostats now available. The Atraugrip* feature keeps the clamp from slipping, and apparently does not injure the vessels. It has a shaft, including the handle, 22 cm. long and its curve is away from the operator so that it may be held by an assistant without obstructing the surgeon's view.

Acetylcholine with magnesium sulfate: In the second group (Table II), magnesium sulfate was used in addition to the 100 mg. of acetylcholine. This was administered by two different methods. In 2 dogs the same procedure as described above was carried out except that, prior to the injection of the acetylcholine, the coronary arteries were perfused with a solution of 2 Gm. of magnesium sulfate. This resulted in various degrees of heart block which reverted to a normal rhythm in 5 to 7 minutes. At this time the acetylcholine was injected with immediate and total standstill for the period of occlusion. In one of these, a normal rhythm was obtained after a short period of massage, in the other the heart stopped in diastole and ventricular fibrillation occurred with massage.

*Patent by Pilling & Co., Philadelphia, Pa.

TABLE II. ACETYLCHOLINE AND MAGNESIUM SULFATE*

ANIMAL	$MgSO_4$ (GM.)	HOW GIVEN	RESULTS
I	2.0	Given i.v. 7 minutes before acetylcholine	Normal rhythm followed by fibrillation in 25 min.
II	2.0	Mixed with acetylcholine	Fibrillation after 4 min. of massage
III	0.4	Mixed with acetylcholine	Fibrillation after 25 min. of massage
IV	0.25	Mixed with acetylcholine	Fibrillation after 1 min. of good beat
V	0.52	Mixed with acetylcholine	Fibrillation before release of inflow
VI	0.39	Mixed with acetylcholine	Normal rhythm
VII	1.0	Mixed with acetylcholine	Fibrillation after 4 min. of occlusion
VIII	2.0	Given i.v. 7 minutes before acetylcholine	Fibrillation with massage

*Acetylcholine, 100 mg. in 8 c.c. volume, perfused into the coronary system in each case to produce arrest.

In 6 other animals magnesium sulfate was perfused through the coronary system in a mixture with the acetylcholine, the amount varying from 0.25 Gm. to 2 Gm. In 4 cases, ventricular fibrillation occurred immediately upon return of circulation or before. In these animals, the hearts were defibrillated by the use of 2 to 3 c.c. of potassium chloride in a concentration of 1.33 mEq. per cubic centimeter perfused into the coronary system. This was followed by an equal volume of 5 per cent calcium gluconate. This was successful in each attempt although the procedure had to be repeated 3 or 4 times in some cases before a normal rhythm was obtained. In 2 of these hearts, there was a spontaneous reversion to fibrillation after a short period of relatively normal contractions.

Acetylcholine with quinidine: In the third group of animals (Table III), quinidine gluconate was given preoperatively in an attempt to prevent fibrillation. The same technique as described under "Method" was carried out except that the animal was given quinidine, 10 mg. per kilogram, intravenously before cooling was started. The quinidine was diluted to 10 c.c. volume with normal saline and was administered over a period of approximately 10 minutes.

TABLE III. ACETYLCHOLINE AND QUINIDINE GLUCONATE*

ANIMAL	RESULTS
I	Spontaneous normal rhythm
II	Spontaneous normal rhythm
III	Spontaneous normal rhythm
IV	Spontaneous normal rhythm
V	Ventricular fibrillation after Adrenalin
VI	Spontaneous normal rhythm
VII	Spontaneous normal rhythm
VIII	Spontaneous normal rhythm

*Quinidine, 10 mg. per kilogram, was given intravenously immediately prior to cooling in each case. Acetylcholine, 100 mg. in 8 c.c. volume, was used to produce arrest.

The animal was then cooled and the procedure completed using acetylcholine for cardiac arrest, which was maintained from 5 to 7 minutes. In each case, the heart maintained good tone during this period of arrest and in all but one animal resumption of normal rhythm was immediate upon the release of inflow

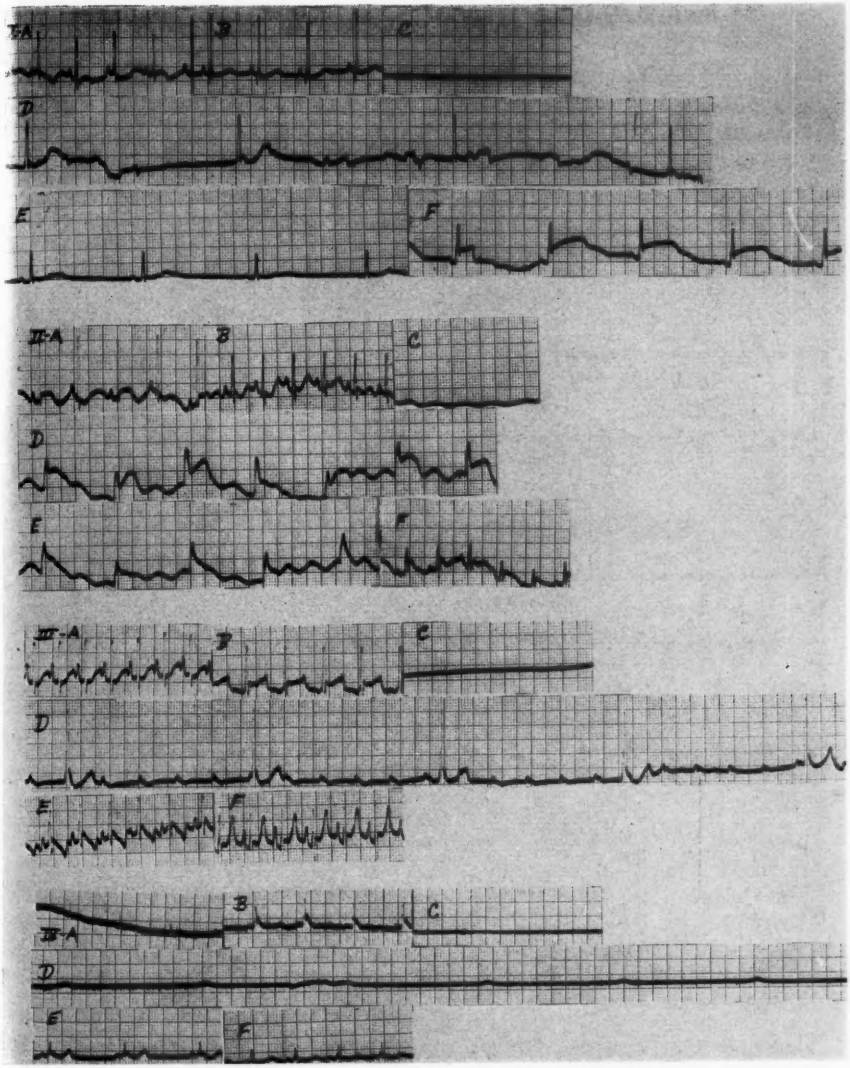

Fig. 2.—Lead II ECG tracings of quinidine animals I-IV. In each case, *A* is a preoperative, normal temperature tracing.

Animal I shows the effects of quinidine in *B*, a prolongation of Q-T interval and elevation of the T wave. Arrest (*C*) is followed by a complete heart block (*D*) which reverted spontaneously to a normal sinus rhythm (*E*). Eight minutes after restoration of circulation there was a normal sinus rhythm with a marked current of injury (*F*).

Animal II shows the same pattern in *A*, *B*, *C*. An idioventricular rhythm with a current of injury (*D*) was established after arrest. Atropine, gr. 1/150, was given 8 minutes later with the establishment of a normal sinus rhythm (*E*). Due to poor tone, Adrenalin 1:1000, 1 c.c., was given 10 minutes after the atropine (*F*).

Animal III shows the "injury potential" at the QRS-ST junction (*B*). Arrest (*C*) was followed by a complete heart block (*D*). This reverted to a normal sinus rhythm in one minute (*E*) and, in 15 minutes, the T waves had become upright.

Animal IV also shows the "injury potential" in *B*. Arrest (*C*) was followed by an idioventricular rhythm originating above the bifurcation with an auricular standstill (*D*). A normal sinus rhythm was established in 5 minutes (*E*). *F* shows the pattern 45 minutes later after the chest was closed.

to the heart and without massage. In one animal, although the heart resumed beating spontaneously after the relase of tourniquets and the clamp, the beats were weak, so one cubic centimeter of 1:1000 Adrenalin was given intravenously whereupon ventricular fibrillation occurred.

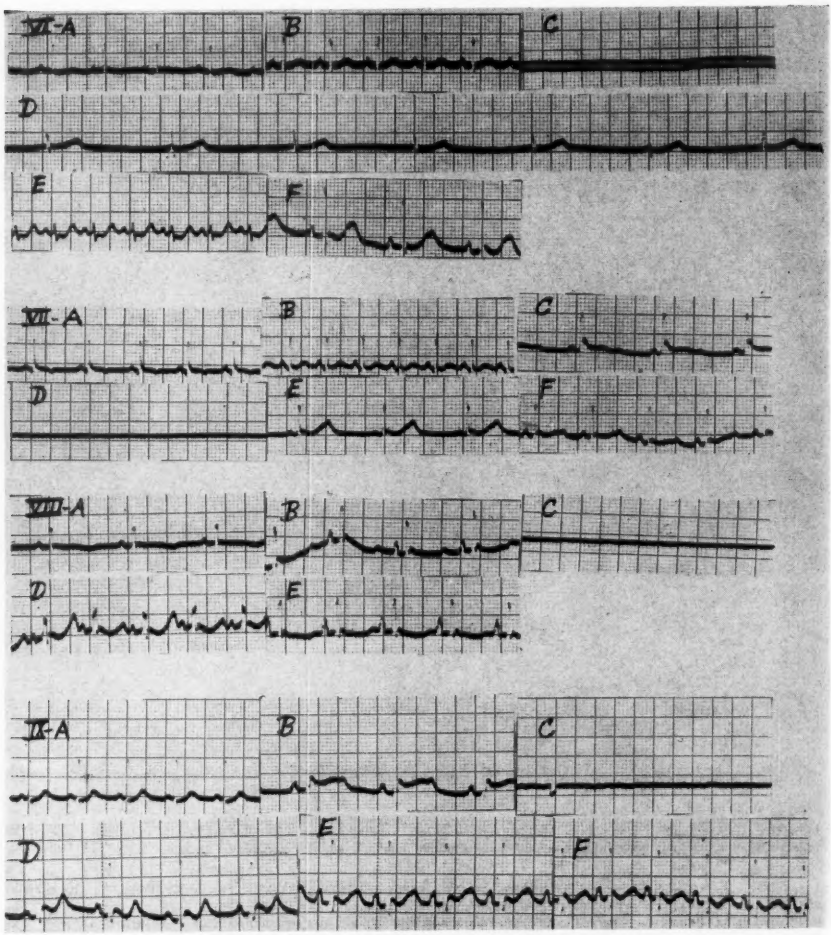

Fig. 3.—Lead II ECG tracings of quinidine animals VI-IX.

Animal VI shows the effects of quinidine (*B*) followed by arrest (*C*). A normal sinus rhythm was established immediately upon restoration of circulation (*D*). *E* shows the effects of atropine and 45 minutes later after these had disappeared (*F*).

Animal VII shows the quinidine effect (*B*) and the "injury potential" at 27° C. (*C*). Arrest (*D*) was followed by a normal sinus rhythm (*E*). *F* shows the pattern one hour later after the chest was closed and the animal warmed to 32° C.

Animal VIII shows the "injury potential" at 28° C. (*B*). Arrest (*C*) was followed by a normal sinus rhythm (*D*). *E* shows the tracing 11 minutes after restoration of circulation.

Animal IX shows the "injury potential" at 29° C. (*B*). Arrest (*C*) was followed by a normal sinus rhythm (*D*). *E* shows the pattern 12 minutes later. *F* is the tracing after incision and repair of the right ventricular wall.

In this group, the right ventricular wall was incised in 4 cases as a stimulus for fibrillation. However, fibrillation did not occur. In 5 of these cases, atrophine, gr. 1/150 in 4 c.c. volume, was perfused into the coronary system before resumption of inflow. This seemed to give a slightly quicker return to normal sinus rhythm. The animals in this group were observed from one day to one month postoperatively with return of normal ECG tracings and grossly normal behavior in all respects.

Figs. 2 and 3 show the ECG tracings of this group of animals except for the case which ended in ventricular fibrillation.

Acetylcholine with Histadyl: In a fourth group of animals, the same technique, as described under "Method," was carried out except that the antihistamine, thenylpyramine (Histadyl-Lilly), was used in conjunction with the acetylcholine (Table IV).

TABLE IV. ACETYLCHOLINE AND HISTADYL*

ANIMAL	HISTADYL (MG./KG.)	HOW GIVEN	RESULTS
I	5.0	Intravenously prior to acetylcholine	Normal rhythm
II	5.0	Mixed with acetylcholine	Fibrillation
III	2.5	Mixed with acetylcholine	Normal rhythm

*Acetylcholine, 100 mg./Kg. in 8 c.c., volume used to produce arrest by perfusion of coronary system.

A normal rhythm was established following standstill in 2 cases. In one of these, 2.5 mg. per kilogram of Histadyl was used in a mixture with 100 mg. of acetylcholine perfused into the coronary system. In the other case, 5 mg. per kilogram of Histadyl was injected into the inferior vena cava immediately prior to the administration of acetylcholine into the coronary system.

In the third case, 5 mg. per kilogram of Histadyl plus 100 mg. of acetylcholine in the coronary system resulted in a complete flaccid standstill which would not revert spontaneously to good contractions with the release of inflow. Massage was required to support the circulation and this precipitated fibrillation. In the 2 cases where a normal beat was obtained, the heart tone was not as good as with the use of quinidine. Also standstill was not as complete and resumption of beats was slower than in the group subjected to quinidine.

DISCUSSION

Ventricular fibrillation is one of the chief complications occurring during hypothermia. In intracardiac surgery, with the use of cardiac standstill, this occurs most frequently when manual massage is required to restore the beat. This is due to the mechanical stimulation of the myocardium as well as to the change in pH and electrolytes. For this reason we felt that if we could protect the myocardium by a depressant we could help overcome this complication.

The effects of quinidine were studied in 9 dogs under hypothermia and cardiac arrest and compared with a series of 9 animals under similar arrest with acetylcholine alone, with a group of 8 animals in which depression of the myocardium was attempted with magnesium sulfate, and with a group of 3 animals in which Histadyl was used.

We have found, contrary to the theory that the magnesium ion is a cardiac depressant, that under hypothermia the irritability of the heart seems to be increased by the use of the magnesium and that it is not protective against ventricular fibrillation. With the use of magnesium, fibrillation occurred much sooner and with less stimulation than in the acetylcholine group.

In most cases, fibrillation can be stopped by the use of potassium chloride and calcium gluconate injected in the coronary system. Good cardiac rhythm can usually be established although this is sometimes done with difficulty and a reversion to fibrillation is common.

In the use of quinidine, one of the main advantages is that arrest in diastole does not occur and the heart resumes regular rhythm without the use of manual massage which is one of the chief causes of fibrillation. Cardiac arrest is produced sooner and total arrest is maintained longer than with the use of acetylcholine alone. This conservation of cardiac energy during occlusion is a factor in decreasing fibrillation. When the factor of cardiotomy is added to those of hypothermia and arrest, quinidine continues to be protective.

Although the work with the antihistamines has not been extensive enough for any conclusions, in the 3 cases where it was used the hearts did not respond as well as with the use of quinidine. The standstill was less complete and restoration of normal rhythm was slower than with the use of quinidine.

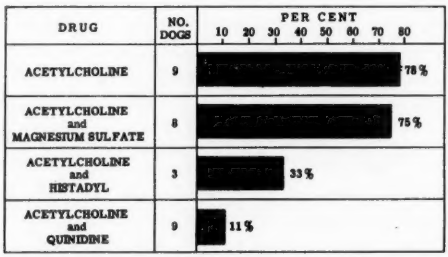

Fig. 4.—Percentage of dogs in which fibrillation occurred subsequent to hypothermia and cardiac arrest induced by acetylcholine alone and acetylcholine used in combination with magnesium sulfate, Histadyl, and quinidine.

Fig. 4 shows the percentage of dogs in which fibrillation occurred subsequent to hypothermia and cardiac arrest in each of the 4 groups of animals we have studied.

ECG tracings were taken of all animals in each group throughout the entire procedure. However, in the interest of brevity and the elimination of repetition, only the tracings of the quinidine group are shown.

SUMMARY

Cardiac arrest was produced in hypothermic dogs with acetylcholine alone and in combination with magnesium sulfate, quinidine, and Histadyl. It was found that the incidence of ventricular fibrillation was not decreased

with the use of magnesium, but that the heart was protected by quinidine and Histadyl. Of these 2 drugs, quinidine appears to be superior although Histadyl was not used extensively and deserves further study. Quinidine decreases the complications of hypothermia.

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THE SURGICAL CORRECTION OF MITRAL INSUFFICIENCY BY USE OF A PERICARDIAL VALVE GRAFT

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A SIMPLE closed procedure has been developed to abolish a regurgitant lesion at the posterior commissure without impairing the functional mobility of the aortic leaflet. This has been accomplished effectively by the addition of a pericardial valve graft to the posterior half of the mural leaflet of the mitral valve.

METHODS

Mongrel dogs, weighing from 20 to 25 Kg., were anesthetized with intravenous Pentothal sodium, after which a left thoracotomy incision was performed through the fifth intercostal space. Mitral incompetence was produced by resecting the posterior portion of the mural leaflet with a mastoid rongeur, after which the chordae in this region were avulsed with a nerve hook.

Initially, an attempt was made to prepare a series of animals with severe chronic mitral insufficiency for future surgical correction. However, production of a major mitral regurgitation was invariably attended by a mortality due to pulmonary edema within 12 to 24 hours. Only insignificant lesions could be produced with survival.

The necessity for the immediate correction of the severe regurgitant lesion became apparent. The present experiment, therefore, comprises a series of animals in which the creation of a significant mitral insufficiency was followed by the immediate insertion of a pericardial valve graft for its correction. Intracardiac pressures from the left atrium and aorta, and an electrocardiogram were obtained before and after the creation of the mitral regurgitation, and again after its surgical correction.

Technique of Creation of Mitral Insufficiency.—The pericardium is opened longitudinally, and a purse-string suture is placed around the base of the left auricular appendage. A Satinsky clamp is placed distal to it, after which the appendage is opened and irrigated with saline (Fig. 1). The bare left index finger is inserted into the atrium, and the mitral valve area is explored. The posterior portion of the mural leaflet is resected with a mastoid rongeur passed transauricularly along the palpating finger. The rongeur is removed, and a nerve hook is similarly introduced. The chordae inserting into the residual

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posterior aspect of the mural leaflet are engaged and avulsed. Upon completion of this procedure, a major regurgitant jet can be palpated in the region of the posterior commissure, thus simulating clinical mitral insufficiency.

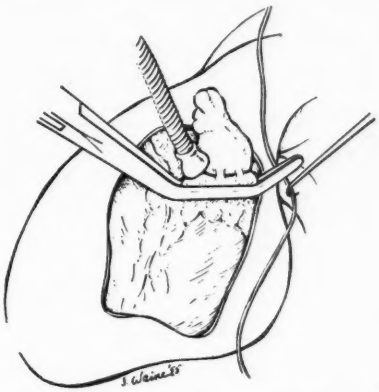


Fig. 1.—A rectangular segment of pericardium is excised for preparation of the graft. A purse-string suture is placed around the base of the left auricular appendage, and a Satinsky clamp is placed distal to it.

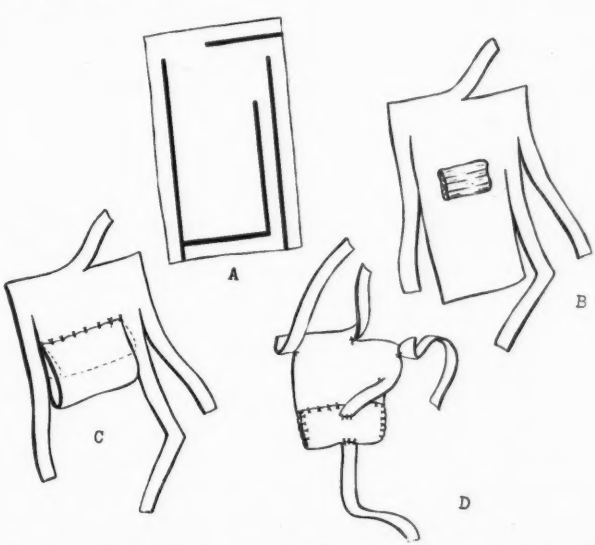


Fig. 2.—*A*, A rectangular segment of pericardium measuring approximately 4 by 7 cm. is secured, and tails are prepared.

B and *C*, A piece of muscle is incorporated into the valve graft to provide the bulk and substance necessary to tamponade the regurgitant jet.

D, Upon completion, a valve graft is created which can be anchored at multiple points along its base, as well as at its apex.

Technique of Repair of Mitral Insufficiency.—A pericardial valve graft is first prepared for insertion (Fig. 2). A rectangular segment of pericardium,

measuring approximately 4 by 7 cm., is secured. Tails are prepared so that the completed valve may be anchored along both its apex and base (Fig. 2, *A*). A piece of muscle is incorporated into the valve graft to provide the bulk and substance necessary to tamponade the regurgitant jet (Fig. 2, *B* and *C*). Upon

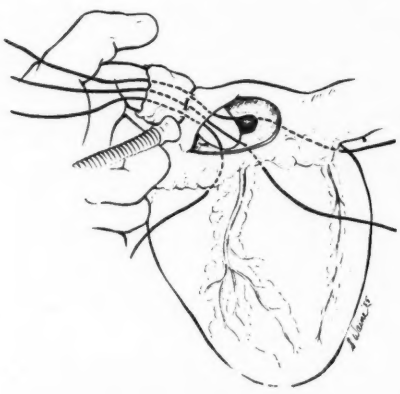


Fig. 3.

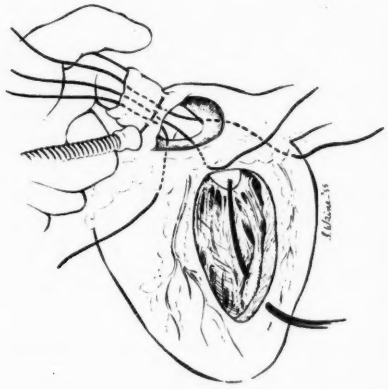


Fig. 4.

Fig. 3.—The first suture is placed posteriorly into the left ventricle just beneath the posterior commissure. It is then passed between the valve leaflets into the atrium, and out through the auricular appendage. The second suture is placed anterior to the regurgitant jet, from below the coronary vessels exteriorly, to the junction of the leaflet with the annulus internally. The third suture is similarly placed midway between the first two.

Fig. 4.—The suture is passed into the posterior papillary muscle for insertion of the graft chordae.

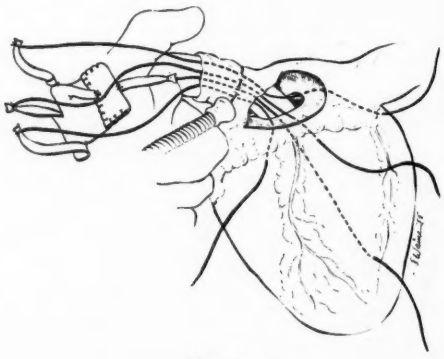


Fig. 5.

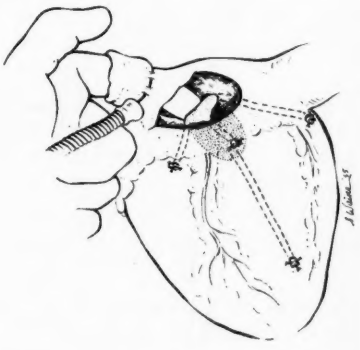


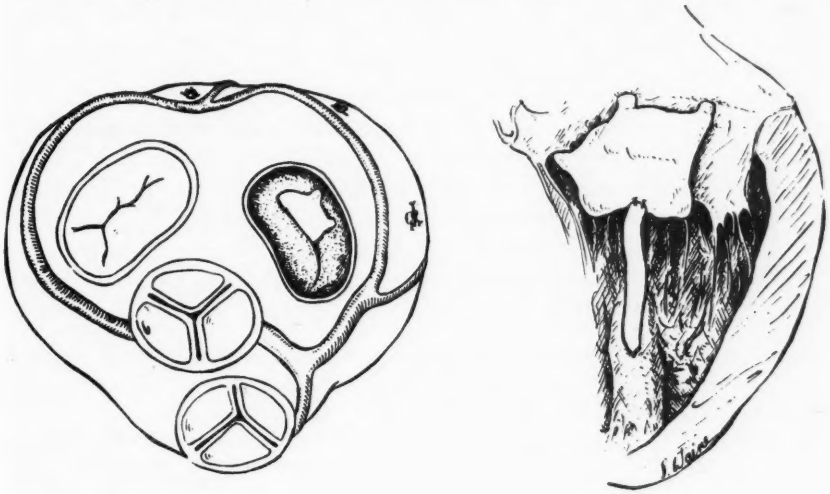
Fig. 6.

Fig. 5.—The sutures are attached to the respective tails of the graft.

Fig. 6.—The pericardial graft is inserted into the atrium and is snugged into its proper position by pulling on the appropriate sutures.

completion, a valve graft is created which can be anchored at multiple points along its base, as well as at its apex (Fig. 2, *D*). The anchorage of the apex into the posterior papillary muscle serves as a chorda tendinea. The bare left index finger is again inserted into the atrium, and the posterior commissure is

located. The first suture* is placed to the right of the posterior descending artery, into the left ventricle just beneath the posterior commissure. The suture then passes between the valve leaflets into the left atrium, and out through the auricular appendage. The end of the suture is immediately attached to the corresponding tail of the valve graft. The next suture is placed in the mural leaflet anterior to the regurgitant jet, at a point approximately midway between the two commissures. This suture is passed from outside the heart just below the coronary vessels, and is immediately angled upward to enter the left atrium at the junction of the valve leaflet with the annulus. This suture, too, is attached to the corresponding tail of the graft. A third suture is similarly placed midway between the first two (Fig. 3). The finger is then



A B

Fig. 7.—*A*, The valve graft is snugged into position so that the regurgitant area is tamponaded.

B, Same, with heart open., demonstrating the final placement of the tails of the graft into the valve leaflet, and papillary muscle.

placed into the left ventricle against the posterior papillary muscle. A suture is passed into the left ventricle at this site, and is guided between the valve leaflets into the atrium (Fig. 4). It is withdrawn from the auricular appendage, and attached to the tail of the valve graft (Fig. 5). The pericardial valve graft is inserted into the atrium and is snugged into its proper position by pulling on the appropriate sutures. The tails are then anchored to the ventricular myocardium (Figs. 6 and 7, *A* and *B*).

In this fashion, a valve graft placed across the posterior portion of the mitral orifice can replace a portion of a resected leaflet of the mitral valve. The bulkiness of the graft immediately tamponades the regurgitant jet without in any way interfering with the mobility of the aortic leaflet.

*Prepared by J. A. Deknatel & Son, Inc., Queens Village, Long Island, N. Y.

RESULTS

1. *Period of Instruction.*—The first series of animals was prepared during the development of the techniques described, with no attempt at survival. Initially, the need for bulk in the graft was not appreciated and, in the first 4 animals, a pericardial valve graft alone, without enclosed muscle, was inserted. The regurgitant lesion remained uncontrolled, and pulmonary edema ensued in all. The placement of the posterior suture proved to be the next troublesome factor. It seemed that regardless of how far posteriorly this suture was placed, the most posterior portion of the mitral orifice could not be tamponaded. This was finally solved by passing the suture to the right of the posterior descending artery, so that it was actually passed into the left ventricle from the external aspect of the right ventricle, through the interventricular septum. Several animals were lost initially, because the necessity for a ventricular tail to maintain the position of the graft was unrecognized. With each ventricular systole, the graft was herniated into the atrium without controlling the regurgitation.

Finally, a group of 6 animals were prepared. Two were sacrificed at 6 months, and 3 at 8 months. One died at 5 months of embolization.

2. *Physiologic Observations.*—In all animals (Table I), after insufficiency was produced, a typical regurgitant atrial pressure tracing was observed. There was an elevation of the atrial C wave (Fig. 9). After the valve graft was inserted, the regurgitant jet was abolished, with reversion of the atrial pressure tracing to normal (Figs. 8, 10).

TABLE I. LEFT HEART PRESSURE AT THORACOTOMY BEFORE AND AFTER INSERTION OF GRAFT

DOG NO.		LEFT ATRIUM (MM. Hg)	PEAK OF C-V WAVE	AORTA	COMMENTS
No. 4	Initial	5-10	10		Complete obliteration of regurgitant jet after insertion of graft
	After regurg.	10-35	37		
	After correction	0-5	5		
No. 2	Initial	7-10	10		Good control of regurgitant jet
	After regurg.	10-30	30		
	After correction	3-7	7		
No. 3	Initial	6-10	10		Good correction of MI with valve graft; minimal residual jet palpable at posterior aspect of mitral orifice
	After regurg.	10-30	30		
	After correction	5-10	10		
No. 1	Initial	5-8	8		Regurgitation well controlled by valve graft; minimal residual jet palpable
	After regurg.	5-25	25		
	After correction	0-5	5		
No. 6A	Initial	5-10	8	120/50	Mitral regurgitation poorly repaired; a large jet was palpable postgraft; the graft was too small and not bulky enough; animal died in 24 hours
	After regurg.	5-20	20	100/44	
	After correction	5-20	20	90/40	

3. *Pathologic Observations.*—In 4 animals, 2 of which were sacrificed at 6 and 8 months, respectively, no regurgitation existed at time of sacrifice. These

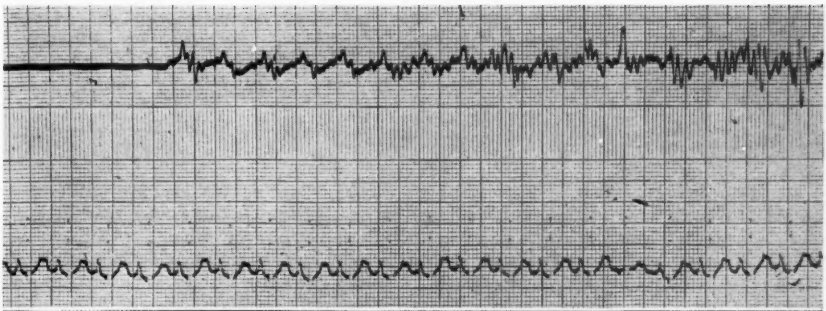


Fig. 8.

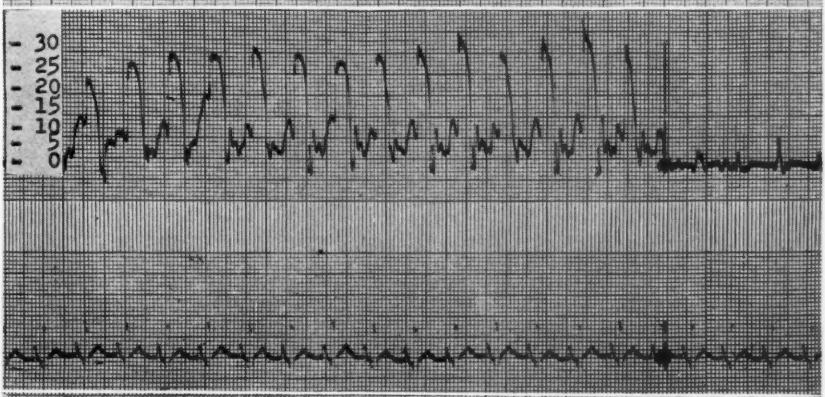


Fig. 9.

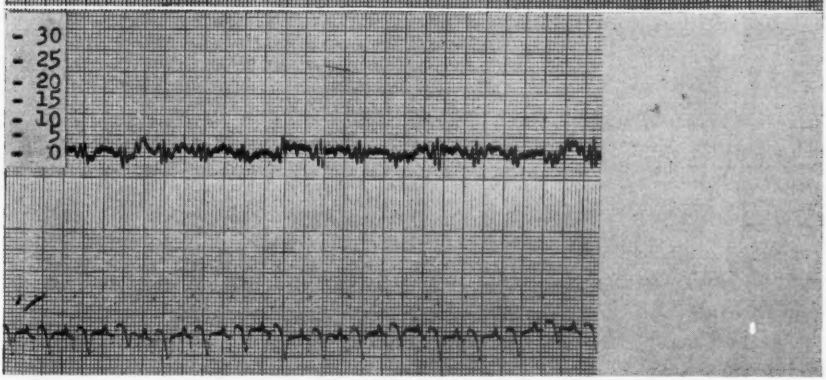


Fig. 10.

Fig. 8.—Normal left atrial pressure tracing taken prior to resection of the mural leaflet of the mitral valve.

Fig. 9.—Same, after production of mitral insufficiency by resection of the posterior portion of the mural leaflet. Note marked elevation of C wave.

Fig. 10.—Same, after insertion of pericardial valve graft. Note complete reversion of pressure tracing to normal.

animals had spent an active postoperative kennel existence. In each, the graft had become adherent to the mitral valve, and completely replaced the resected portion of the leaflet. The base of the graft was entirely adherent to the annular attachment of the valve. The apical chorda was thickened and fibrotic. The graft seemed to have completely and effectively replaced the resected portion of the valve (Fig. 11).

In one animal sacrificed after 6 months, although the major regurgitant jet had been abolished, a residual fine jet could still be palpated. In this animal the valve graft was found to be in proper position, but the base was adherent only at its points of fixation. The regurgitant jet, palpated prior to sacrifice, had emerged between the points of fixation. This finding led to the fixing of the base of the graft at four points in the ensuing experiments.

Fig. 11.—Same dog, 8 months postoperative. The graft has completely replaced the resected portion of the mitral valve leaflet. The base is entirely adherent to the annular attachment of the valve. The apical chorda is thickened and fibrotic.

One animal died after 5 months, of peripheral embolization, including a terminal saddle embolus. Post-mortem examination revealed the base of the graft to have been avulsed at two points of fixation. The pericardial flap was found in the ventricular chamber, fixed at its apical portion, and surrounded by old and recent thrombus. This thrombus was the obvious source of the peripheral emboli.

DISCUSSION

Mitral insufficiency may vary in character as well as in degree. It may be a minor lesion associated with a predominant stenosis, the orifice of which is maintained by a thickened fibrous, or calcific ring. It may be considerably advanced, but still associated with moderate stenosis at the anterior commissure, or it may be the sole and major lesion of the mitral valve. In the latter

two categories, the regurgitant jet is found posteriorly, emerging from the region of the posterior commissure. Invariably, valvular competence is maintained anteriorly.

Bailey[12] believes that normally, although there is a considerable excess of valve leaflet for coaptation anteriorly, there is very little such excess tissue posteriorly (Fig. 12). This relationship is seriously altered by the thickening, rolling, and shortening of the valve leaflets and chordae, caused by the rheumatic infection. The anterior portions of both the mural and septal leaflets, having an excess of valve tissue, seem to tolerate this shortening without loss of competence. The posterior portions of these leaflets, however, barely coapting in the normal state, are rendered incompetent by this pathologic process. In

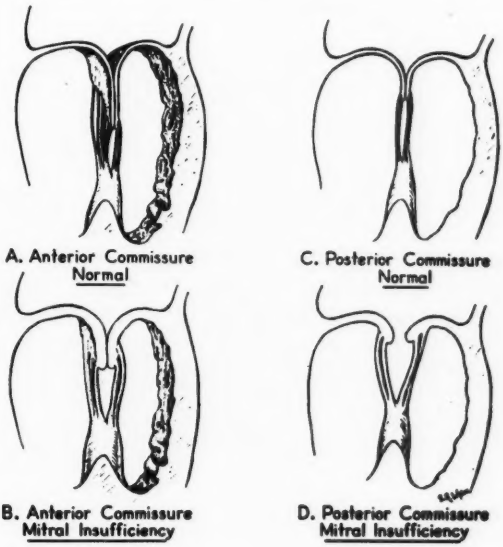


Fig. 12.—The regurgitant jet invariably emerges through the posterior commissure. Note the apparent deficiency in leaflet of the posterior portion of the mural leaflet. Compare to Fig. 7,*A* postoperatively.

truth, there seems to be an actual deficiency of valvular substance of the posterior aspect of the mural leaflet, which may be so severe that only a residual rim of atrophic tissue remains. The physiologic sequelae of the regurgitant lesion revolve about the increased burden placed upon the left ventricle, which becomes dilated and hypertrophied. This is then followed by a secondary dilatation of the mitral annulus.

It would seem, therefore, that the surgical correction of mitral insufficiency must be directed toward the addition of substance to the posterior portion of the deficient mural leaflet. This valve substance must tamponade the regurgitant flow of blood by enabling the posterior portion of the aortic leaflet to coapt

against it during ventricular systole. At the same time, it has become obvious that the mobility of the aortic leaflet cannot be impaired without lethal consequences.

There have been many previous attempts at the surgical correction of mitral insufficiency, starting with Murray, Wilkinson, and McKenzie,[1] who first attempted to replace damaged cusps with vein grafts in 1938. Templeton and Gibbon,[2] in 1949, next attempted to replace segments of the tricuspid valve with venous or pericardial grafts, using an open right atriotomy. Bailey and co-workers[3, 4] attempted to occlude the regurgitant mitral orifice using a transventricular pericardial sling intended to act as an intermittent ball valve during ventricular systole. Johns and Blalock[5] reported this technique, but used a

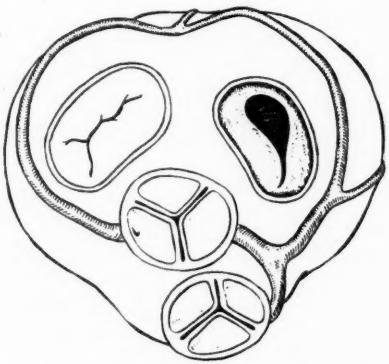


Fig. 13.—*A*, Normally, there is an excess of valve tissue for coaptation anteriorly. *B*, Rheumatic valvulitis is accepted anteriorly without regurgitation because of the excess of substance. *C*, Posteriorly, the valves barely coapt, and there is little overlap of tissue. *D*, Posteriorly, however, where there is little room for leeway, loss of valve substance leads to failure of coaptation of the leaflets.

polyvinyl sponge prosthesis. Bailey and colleagues[6] next attempted to suture the posterior aspects of the mitral leaflets together. This technique must have immobilized the aortic leaflet. Harken[7] and Carter[8] and their associates inserted plastic prostheses into the ventricular chamber in an attempt to control the regurgitation in flutter-valve fashion. Glenn and co-workers[9] attempted to tamponade the regurgitant jet with a transchamber, vertically suspended, intracardiac graft. Davila,[10] on the other hand, has attempted to approach the problem from the reverse aspect of diminishing the size of the mitral orifice by use of a circumferential suture.

It seems that the procedures devised fit into three categories. The first revolves around the development of a transventricular flutter-valve designed to occlude (intermittently) the regurgitant portion of the mitral orifice. The valves inserted have been pericardial or prosthetic. The pericardial grafts become thickened, fibrotic, and attenuated.[11] The foreign bodies become fibrotic and, in a short period, both become immobile and useless. The second consists of an attempt to diminish the circumference of the mitral orifice. This method

SCHOOL OF MEDICINE

seems to ignore the basic anatomic and physiologic hemodynamic aberration seen in mitral regurgitation. The third type of surgical attack revolves about a recognition of the primary anatomic deficiency in mitral insufficiency, namely that of an absolute loss of valve substance.

During cardiotomy for predominant mitral stenosis associated with insufficiency, it has been recognized that the regurgitant jet almost invariably emerges through the posterior commissure (Fig. 13). Proper placement of the exploring finger in this region can effectively tamponade the regurgitant jet, as evidenced by a rise in systemic pressure and an increase in the fullness of the peripheral pulse. This fact, coupled with the pathologic finding of an absolute deficiency of valvular substance of the posterior portion of the mural leaflet, has led to the concept of tamponading the regurgitation by the proper placement of a valve graft which would adhere to, and add substance to, the atrophic portion of the mural leaflet.

Experience has demonstrated that the mobility of the aortic or septal leaflet cannot be impaired. This fact has led to the inevitable development of a valve graft positioned to add substance to the posterior portion of the mural leaflet, and thus effectively tamponade the regurgitant jet. The operation for the insertion of the valve graft is simple, and permits the utilization of a closed technique. The diagonal placement of the graft prevents the future development of a stenosis of the orifice by, at all times, ensuring full mobility of the aortic leaflet. In all animals, the graft is incorporated into the substance of the mural leaflet.

Undoubtedly, with the advent of open heart surgery, it will be possible to position this valve graft with even more accuracy.

SUMMARY

A closed technique is described for the placement of a pericardial valve graft into the orifice of the mitral valve for the control of mitral insufficiency.

The valve tamponades the regurgitant jet in the region of the posterior commissure, and adds substance to the deficient portion of the posterior aspect of the mural leaflet.

The valve is well tolerated, and has been incorporated into the substance of the mural leaflet.

The results of this experiment justifies the use of this technique in patients with regurgitant lesions of the mitral valve.

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BENIGN, PEDUNCULATED, INTRALUMINAL TUMORS OF THE ESOPHAGUS

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POLYPOID, intraluminal tumors were among the first benign esophageal neoplasms to be described. Despite their infrequent appearance, they are of considerable interest because of the sensational manner in which they may appear (by regurgitation of the growth) and because, if untreated, they may result in death of the patient. Yet they are amenable to curative surgical removal.

According to Harrington,[3] Sussins is credited with one of the first necropsy descriptions of an esophageal polyp (1559). In 1871, Coats[2] described the necropsy findings in a patient who died with esophageal obstruction secondary to what he called an "intraluminal polypoid myxoma." He noted the benign nature of the lesion, emphasized its narrow band of attachment, and speculated about a possible cure of such a condition by surgical removal. The fact that these intraluminal esophageal tumors have been diagnosed infrequently is illustrated by a review by Totten and associates,[7] in 1953, wherein it is noted that they were able to find only 40 such cases recorded in the literature. The surprising appearance of the regurgitated tumor in the mouth of the patient occasionally facilitated the diagnosis. Successful surgical removal was first recorded in the American literature by Vinson[8] in 1922. The patient was the first of 6 who have been seen and treated by operation at the Mayo Clinic. With the exception of 2 cases, all have been reported previously in the literature.[3, 4] The pertinent clinical data in the 6 cases are summarized in Table I. Reports of the 2 most recent cases of these unusual esophageal tumors encountered at the Clinic follow.

REPORT OF CASES

CASE 1.—A 56-year-old man was first seen at the Clinic in 1951, at which time he complained of dysphagia of 6 months' duration with associated anorexia and loss of 48 pounds. X-ray examinations conducted by his home physician had revealed dilation of the esophagus, and esophagoscopic examination had given negative results. Gradually the patient had experienced intermittent regurgitation and increased substernal distress on swallowing. Dysphagia became so severe that he had had to be fed by tube for 2 weeks. When the tube was removed the patient had little trouble with swallowing for 6 weeks, but the symptoms of dysphagia, substernal fullness, regurgitation, and weakness returned.

The patient's medical history and a review of symptoms contributed nothing of significance.

From the Mayo Clinic and Mayo Foundation.
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TABLE I. SUMMARY OF CLINICAL DATA IN SIX CASES

PERTINENT DATA	CASE NUMBER					
	1	2	3	4	5	6
Age; year encountered	62 yr. (1921)	24 yr. (1940)	42 yr. (1943)	21 yr. (1944)	56 yr. (1951)	25 yr. (1955)
Sex	Male	Male	Male	Male	Male	Female
Chief complaint	Coughed up growth	Sore throat	Regurgitation	Dysphagia	Dysphagia	Dysphagia
Duration	6 yr.	3½ yr.	8 yr.	10 yr.	6 mo.	1 yr.
Symptoms:						
Dysphagia	No	Yes	No	Yes	Yes	Yes
Vomiting	Yes	No	Yes	Yes	Yes	Yes
Pain	No	Ache beneath lower part of sternum on swallowing	Substernal pressure	Substernal, on swallowing	Substernal fullness	Substernal pressure
Loss of weight	30 pounds	12 pounds	30 pounds	20 pounds	48 pounds	19 pounds
Respiratory	No	Productive cough	Dyspnea, pneumonia	No	No	No
Melena	No	Yes	No	No	No	No
History of regurgitated tumor	Yes, twice	Yes, 4 times	Yes, once	Yes, many times	No	No
X-ray diagnosis		Cardiospasm	Cardiospasm	Intraluminal polypoid tumor	Large intraluminal mass	Cardiospasm with large intraluminal foreign body
Esophagoscopic finding	Intraluminal polyp	Intraluminal polyp	Intraluminal polyp	Intraluminal polyp	Intraluminal polyp	Intraluminal polyp
Therapy	Excision	Excision	Excision	Excision	Excision	Excision
Route of excision	Cervical	Cervical	Right transpleural	Oral	Cervical	Right transpleural
Level of tumor attachment	Just below introitus	Just below introitus	Just below introitus	Just below introitus	Just below introitus	Level of azygos vein
Postoperative complications	None	Paralysis left vocal cord	Empyema	None	None	Micrococcal enteritis
Result	Died in 6 months of abdominal carcinomatosis	Well	Well at last report	Well	Well	Persistent dysphagia months later; well at last report

Physical examination revealed evidence of much loss of weight and mild edema of the lower extremities, but otherwise no abnormalities were noted.

Laboratory studies disclosed a concentration of hemoglobin of 11.4 Gm. per 100 c.c. of blood and leukocytes numbered 13,500 per cubic millimeter of blood with some shift to the left noted on the differential blood smear. Urinalysis gave normal results. The sedimentation rate of erythrocytes was 53 mm. in one hour (Westergren method). X-ray examination of the thorax did not reveal any abnormality. By means of contrast medium, the roentgenologist observed evidence of a large intraluminal mass in the mid-portion of the esophagus (Fig. 1). At the time of esophagoscopic examination, a pedunculated tumor was noted arising just below the esophageal introitus from the posterior and right lateral walls of the esophagus. The tumor was lobulated and extended down into the lower third of the esophagus. It was the esophagoscopist's opinion that this was a large, pedunculated, intraluminal fibrolipoma.

Fig. 1.—Well-delineated intraluminal polyp of the esophagus.

A cervical approach was used and the lesion, which measured 11 by 2 by 1.5 cm., was excised (Fig. 2). The pathologist reported the tumor to be a fibrolipoma (Fig. 3). The postoperative course of this patient was uneventful and follow-up studies showed that 6 years later he continued to be free of symptoms.

CASE 2.—A 24-year-old woman was first seen at the Clinic in March, 1955, at which time she complained of progressive dysphagia of 13 months' duration. Initially, in February, 1954, she had noted only slight difficulty in swallowing solid food which was minimized by washing the food down with liquids. In a few months, however, the dysphagia had increased and she had sought the advice of a physician on two occasions. Without benefit of x-ray examination, the patient was told that her symptoms probably were due to increased "nervous

Fig. 2.—Lobulated fibrolipoma with long pedicle of attachment.

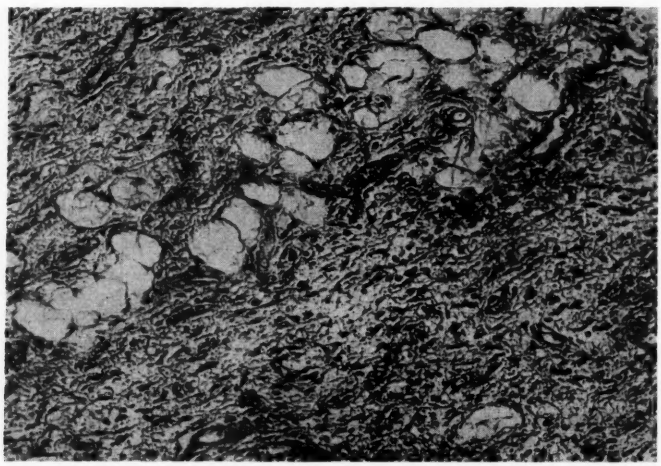

Fig. 3.—Representative area of fibrolipoma (hematoxylin and eosin; ×155).

tension.'' Soon she began to regurgitate much of the food she swallowed, so that by February, 1955, her diet was limited to liquids. Medical aid was sought again and x-ray studies of her esophagus, as well as an esophagoscopic examination, were done with the resulting diagnosis of cardiospasm. Dilation did not provide relief of her symptoms and she began to experience substernal fullness and aching when she swallowed. She had lost 19 pounds in 3 months.

The medical history and a review of symptoms contributed nothing, with the exception of some emotional problems that were of sufficient severity to require consultation with a psychiatrist.

Physical examination at the Clinic revealed a tense, pale young woman who had obviously lost some weight, but no other abnormality was noted.

Fig. 4.—Note the marked dilation of esophagus associated with this intraluminal polyp.

Routine laboratory studies disclosed a concentration of hemoglobin of 11.7 Gm. per 100 c.c..of blood; erythrocytes numbered 3,720,000 and leukocytes 6,100 per cubic millimeter of blood with a normal differential count. The sedimentation rate of erythrocytes was 60 mm. in one hour (Westergren). Serologic tests and routine urinalysis gave negative results. X-ray examination of the thorax revealed the lung fields to be clear. Abnormality of the chest wall (pectus excavatum) was noted. X-ray studies of the esophagus with contrast medium showed a markedly dilated esophagus and the presence of an intraluminal foreign body that measured 15 by 7 cm. (Fig. 4). Cardiospasm was suggested by the roentgenologist. At the time of esophagoscopic examination (H. A. A.), a large, intraluminal polyp was noted with an attachment arising from the posterior wall of the esophagus, about 10½ inches from the upper teeth. Fairly large blood vessels were noted on the surface of the tumor stalk. On April 2, 1955, a transpleural excision of the lesion was accomplished through a right fifth interspace incision (F. H. E.). The tumor extended from its attachment just above the level of the azygos vein to just above the diaphragm. The esophagus was markedly dilated throughout this distance. The tumor measured 14 by 7

Fig. 5.—Intraluminal polyp with ulceration at its distal end.

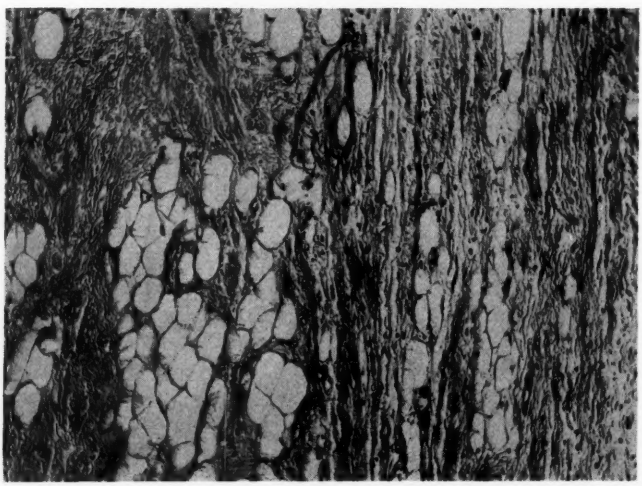

Fig. 6.—Intermixture of fatty tissue and fibrous stroma typical of benign intraluminal esophageal polyps (hematoxylin and eosin; ×100).

by 5 cm. The mucous membrane was intact over the somewhat lobulated surface with the exception of an area of ulceration at the distal end of the tumor (Fig. 5). The microscopic character of the tumor is shown in Fig. 6.

The patient's early postoperative course was complicated by enteritis due to *Micrococcus pyogenes*, which responded quickly to erythromycin therapy. She had no difficulty swallowing. X-ray studies of the esophagus 2 weeks after operation showed the esophageal dilation to persist, with some delay of barium at the esophagogastric junction. Studies of esophageal motility showed that the gastroesophageal junctional region failed to participate in the swallowing reflex and also showed failure of the primary peristaltic wave. Methacholine chloride (Mecholyl) injected subcutaneously did not elevate the intraluminal pressure of the esophagus. It was impossible to conclude definitely whether this patient had primary achalasia also, or whether these findings were all due to prolonged esophageal dilation and operative trauma.

For 5 months the patient ate normally and during this period she gained 20 pounds. In October, 1955, she again noted the onset of dysphagia and regurgitation similar to her preoperative symptoms. She was re-examined and roentgenograms of the esophagus showed evidence of some dilation but very little delay of barium at the esophagogastric junction. Repeat studies of esophageal motility showed the cardia to be nonfunctioning and incompetent, and, in comparison to the previous studies, suggested a "muscular or nervous" degeneration of the esophagus with changes too extensive to be accounted for by the operation. Esophagoscopy revealed the lower portion of the esophagus to be atonic with redundancy of the esophageal mucosa. A sound, size 50 Fr., was passed into the stomach without difficulty.

In February, 1957, this patient reported her health to be good and she no longer suffered from dysphagia.

ETIOLOGIC ASPECTS

It has been proposed that in view of the usual high midline origin of these strange esophageal lesions they may represent a developmental anomaly of one of the branchial arches.[6] There is little support for such conjecture. Practically speaking, with some proliferation of tissue in the loose submucosal area of the proximal esophagus, one can visualize how the propulsive movements of swallowing could play a significant role in the development of these tumors. From the available gross and histologic evidence, it seems most reasonable to include these lesions as true neoplasms rather than unusual inflammatory reactions.

PATHOLOGIC FINDINGS

Pathologically, these tumors comprise a somewhat heterogenous group. This is apparent from the variety of pathologic terms employed in the literature to classify these unusual lesions, including fibromas, lipomas, myxomas, leiomyomas, myomas and various combinations of these terms. Grossly, the lesions are all elongated to some degree, presumably because of the molding effect of the esophageal wall. The surface of the tumor may be irregular and lobulated, and occasionally it is distinctly a multilobed structure arising from a common pedicle. Multiple tumors have been found to occur in the same patient.[5] The mucous membrane of squamous epithelium is usually intact over the surface of the tumor. Ulceration of the surface may occur secondary to the trauma of swallowed food, or as a result of peptic digestion of the distal end of the growth which may protrude through the cardia. Microscopically

these tumors present a mixture of loose, fibrous tissue associated with myxomatous and fatty changes. Inflammatory reaction may be evident in the vicinity of surface ulceration. It would seem most descriptive and convenient to designate the group histologically as fibrolipomas.

CLINICAL MANIFESTATIONS

The commonest clinical manifestations of these intraluminal, polypoid growths result from obstruction of the lumen of the esophagus. Dysphagia, regurgitation and vomiting may be intermittent, but the reduction in intake of food is such that significant loss of weight usually occurs. The average loss in this series of patients was 25 pounds. Most of the patients complained of substernal distress of some type. An uncomfortable feeling of substernal fullness is a common complaint, but some patients describe pain very suggestive of angina. Respiratory symptoms, consisting of cough, dyspnea, recurrent infection and even hemoptysis, may arise as a result of aspiration of esophageal contents or compression of the tracheobronchial tree. Ulceration of the surface of the tumor may manifest itself in melena or hematemesis. The most dramatic evidence of the lesion is its appearance in the patient's mouth with coughing or regurgitation.

DIAGNOSIS

As a group, these patients have presented perplexing diagnostic problems. The history may be only suggestive, or it may be diagnostic with the story of a regurgitated tumor on one or more occasions. This was true in 4 of the 6 patients in this group. A roentgenogram of the thorax may exhibit widening of the mediastinal shadow as a result of the tumor and associated dilation of the esophagus. Ingested barium may divide at the level of the mass and delineate its borders precisely. Along with this evidence the roentgenologist may then note movement of the tumor and irregularities of the peristaltic wave above the tumor at the level of attachment of the pedicle. Occasionally the esophagus may be greatly dilated and the intraluminal tumor can be mistaken for a large foreign body. This is illustrated by the fact that 4 of the 6 patients in this series were thought to have cardiospasm.

Esophagoscopy may be the most precise means of diagnosis. Some of our patients, as well as many of those whose cases are reported in the literature, had undergone this procedure on more than one occasion. The growth was overlooked because the examiner was misled by the intact mucous membrane over the intraluminal tumor. The endoscopist may first discover the tumor at its distal end. The remainder of the tumor, its pedicle and attachment may then be visualized by appropriate maneuvers.

TREATMENT

The indicated treatment is surgical removal. These tumors have been excised by oral, cervical, and thoracic approaches. The oral route may be technically feasible if the tumor can be delivered into the mouth; this approach

was used in one case in this series. However, vessels in the pedicle may present problems of hemostasis and it would seem more reasonable to approach this usual site of attachment of the pedicle more directly through a cervical incision. Occasionally the attachment will be in the thoracic portion of the esophagus and, depending on the level, an approach through either the right or left pleural space should permit easy removal of the intraluminal tumor.

PROGNOSIS

Without a diagnosis and removal many persons having these benign intraluminal tumors have died from complications owing to the lesion. Totten and associates noted that of 40 patients having such growths, a third died as a direct or indirect result of the tumor and in most cases the diagnosis was incorrect. Complete respiratory obstruction at the laryngeal level may be produced by regurgitation of the mass. Chronic esophageal obstruction with dilation of the lumen can be associated with intermittent aspiration of esophageal contents and pneumonitis, bronchiectasis, pulmonary abscess or other serious suppurative complications.

With surgical removal of the growth, one would expect complete relief of symptoms. This has been true in a majority of patients, but some have continued to have symptoms related to esophageal dysfunction. The dilated esophagus may not assume normal proportions, as illustrated in the case of the most recent patient in this series. This young woman continued to complain of intermittent dysphagia and regurgitation, and x-ray studies revealed persistent, moderate dilation of the esophagus without much delay in transit of the barium at the esophagogastric juncture. Studies of esophageal motility revealed some characteristics of cardiospasm, but these were not sufficiently typical to be diagnostic. One could conjecture a secondary degeneration of myenteric plexuses from the prolonged esophageal dilation, or a primary achalasia as an associated condition. Unfortunately a portion of the esophageal wall of this patient was not removed for study. She continued to have dysphagia and occasional regurgitation; repeated studies of esophageal motility a few months later revealed even more abnormalities of function and suggested a "progressive muscular or nervous degeneration." It is possible that irreversible changes in the wall of the esophagus occurred with its prolonged dilation. Beeler and associates[1] reported that cardiospasm is not uncommonly associated with long intraluminal tumors. Studies of esophageal motility do not support such a coincidence and we would suspect these patients to have problems similar to those of the patient described in the second case reported herein.

SUMMARY

Benign intraluminal esophageal tumors may result in distressing symptoms for the patient and can present perplexing diagnostic problems for the physician. X-ray and esophagoscopic examinations may precisely delineate the origin and extent of the lesion and surgical removal can be accomplished with

minimal risk. With excision of the growth, complete relief of symptoms is usually attained, but derangement of esophageal function may prevent a completely satisfactory result for the patient.

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IVALON GRAFT TO BRIDGE CORONARY ARTERY OCCLUSION

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IN one hundred consecutive autopsy specimens we found that the majority of patients who die of coronary heart disease have a short intraluminal obstruction near the origin of a major artery. The artery distal to the occlusion is frequently sufficiently free of compromise of lumen to supply adequately enough blood flow to nourish the myocardium. The ideal surgical attack on this problem would be to open the coronary artery at the point of obstruction, ream out the atherosclerotic block, and close the incision. However, currently, the small size of the vessel and the technical problems involved militate against this direct approach, enticing though it is. Further, if the obstruction is complete, death of peripheral myocardium would make such an endarterectomy of little or no use to the infarcted area. Also, atherosclerosis is not generally confined to a solitary coronary artery but is a generalized process and further obstruction can occur subsequently in another artery.

Many other methods of revascularization have been suggested. In our hands the most promising technique is cardiopneumopexy, developed in this laboratory, a desirably simple procedure with a low mortality rate equal to only 6 months of medical treatment. This method consists of wide incision of the pericardial sac, phenol epicardiolysis, light asbestos poudrage and suturing the lung to the myocardium or inner surface of the adjacent pericardium.[1, 2] Over the past 5 years we have studied this procedure extensively utilizing 187 dogs and have employed it clinically 21 times with encouraging results. However, it is no panacea, but a valuable adjunct to existing medical therapy for coronary heart disease. Furthermore, a minimum of another 10 years of clinical observation is necessary before final conclusions as to its efficacy can be drawn.

In an experimental effort to attack this problem of coronary occlusion in more direct fashion, we proposed an Ivalon graft as a shunt between the left subclavian artery and a coronary artery beyond the point of an acute obstruction.

TECHNIQUE

In this procedure the left chest wall is opened by posterolateral incision through the fourth interspace. The pericardium is opened widely and the

This research was carried out under a grant of the Washington State Heart Association. The research laboratories of the Seattle Veterans Administration Hospital were used for the experiments.

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subclavian artery isolated in the neck. The left anterior descending coronary artery is elevated from its bed. The subclavian artery is severed between patent ductus clamps, the distal end doubly ligated, and the proximal end anastomosed to the large end of the tapered Ivalon graft. Then with a scalpel, a nick is made in the coronary artery. The smaller end of the graft is inserted distally and fixed in position by a simple silk ligature. The coronary artery is then tied off proximad the anastomosis (Fig. 2). The lung is expanded and the chest closed in the usual fashion.

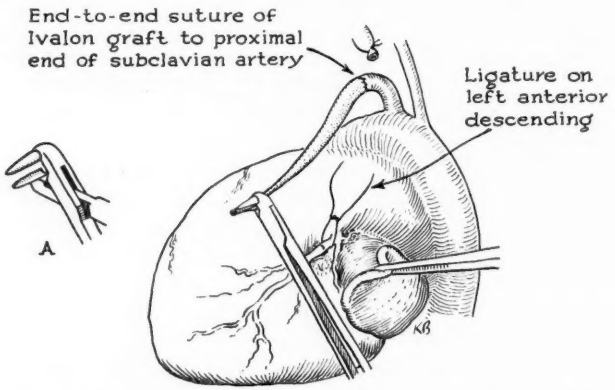

Fig. 1.—This sketch denotes the view of the heart obtained through a left posterolateral incision through the fourth interspace. One can see the short left coronary artery with its two major branches, the left anterior descending and the circumflex arteries. These are readily visible when the auricle is elevated. In this particular technique the subclavian artery is cleanly separated from its surrounding tissue in the neck and severed between patent ductus clamps. The distal end is doubly tied and permitted to retract into the neck. The proximal end is anastomosed end-to-end to the large end of the Ivalon graft. The left anterior descending coronary artery is then elevated from its bed and cleaned over a distance of approximately 1.5 cm. and a transverse nick made in it on the anterior surface for introduction of the distal end of the graft.

A very useful instrument, developed by one of the authors (D. M.), has been found to be of considerable help in introducing the distal end of the Ivalon graft into the very small-bore coronary artery (Fig. 1). It has the advantage of holding the coronary artery wide open and permitting rapid introduction of the graft.

In this series we operated on 18 dogs. The first 5 dogs constituted efforts to evolve a technique and actually are not considered a part of the present statistics. Of the next 13 dogs, on whom the standardized procedure was used, 7 or approximately one half died the day of surgery, generally from ventricular fibrillation when the left anterior descending coronary artery was tied. The remainder were sacrificed 4 to 10 weeks later. In 4 of these there was evidence of at least subendocardial infarction and, in some instances, more extensive infarction of the myocardium. The Ivalon graft usually was patent and contained at the most some jelly-like material. In only one instance was there obstruction by thrombus of the subclavian artery-Ivalon graft anastomosis. It was the impression of the investigators that the problem in this technique is to get blood to flow through the peripheral myocardial field, beyond the point

of anastomosis of graft to coronary artery. This obstacle was present in each instance in spite of the use of heparin at the time of surgery. The advisability of using more prolonged anticoagulant therapy, employing either heparin or Dicumarol, was considered but rejected.

Actually a higher percentage of dogs survived this procedure than in our control series in which 3 out of 4 dogs succumbed to ligation of the left anterior coronary artery.[2]

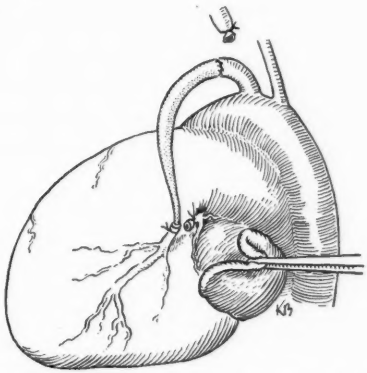

Fig. 2.—This depicts the graft in situ. The left anterior descending coronary artery is ligated securely proximal to the anastomosis to produce an acute coronary occlusion of substantial dimensions in a heart not given the advantage of gradually developing anastomotic channels.

MATERIAL

Ivalon is a polyvinyl sponge found to be biologically inert and, when implanted in tissue, is rapidly invaded by a noninflammatory type of fibrous tissue. Ivalon is formed by hardening foamed polyvinyl alcohol with formaldehyde.

Preparation of the Ivalon graft has been standardized in this laboratory. Ivalon surgical sponge is supplied commercially sealed in a plastic film bag with a small amount of glycerol (hygroscopic agent) and a trace of the formaldehyde that was used in polymerization. Before use it must be thoroughly washed free of these contaminants. This may be done by leaving in running tap water for several hours or by rinsing and wringing 30 to 50 times.

After thoroughly washing it has been our practice to allow the sponge to air-dry for several days, after which time it is quite rigid. For this particular use we cut the sponge into slabs that measure some $\frac{3}{16}$ inch thick when wet. The slabs are scissor-cut into strips the length of the sponge and $\frac{1}{2}$ inch wide. After soaking in warm water, these strips are ready for fabrication.

To adapt the grafts to the wide variations in anatomy they are made into a tube that tapers from $\frac{3}{8}$ inch to $\frac{3}{64}$ inch in $2\frac{1}{2}$ inches and then remains constant for $1\frac{1}{2}$ inches. The wall thickness is approximately $\frac{1}{32}$ of an inch. This configuration is obtained by wrapping the strips in a spiral around a polished brass form, compressing the Ivalon with a 0.006-inch strip of polyvinyl film twice, and fixing the Ivalon with heat (boiling water).

We use one 10-inch length of 0.006 by ½ inch polyvinyl film for each graft and one 8½-inch strip of Ivalon, 3/16 inch thick and ½ inch wide.

Some silicone-lined grafts were prepared but these seemed to be of no greater value than the standard graft.

SUMMARY

In an effort directly to attack the atherosclerotic intraluminal obstruction in coronary occlusion we have investigated the use of a tapered Ivalon graft, shunting blood from the left subclavian artery to the left anterior descending coronary artery distal to a complete acute obstruction. More dogs have lived following this procedure than in the control series of ligations. Nevertheless, in none of these dogs was circulation through the graft maintained for any great length of time. The problem of anastomosis of grafts to small-bore arteries has not been solved as yet.

At this stage we feel that an Ivalon graft to bridge such a block is not a clinically feasible solution to coronary artery obstruction and that cardiopneumopexy is a more successful and desirable procedure. Furthermore, coronary disease is multicentric and further occlusions could occur in another artery. However, we hope that eventually direct attack on the obstruction with removal of the atherosclerotic plaque will be possible to aid those patients with an incomplete block and in whom the myocardium supplied by that vessel is intact as yet. This series is intended as a steppingstone toward that goal.

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PULMONARY ARTERIOVENOUS FISTULA ASSOCIATED WITH CAPILLARY TELANGIECTASIA (RENDU-OSLER-WEBER DISEASE): REPORT OF A CASE ILLUSTRATING USE OF METAL CASTING FOR DEMONSTRATING THE LESION

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NEW YORK, N. Y.

PULMONARY arteriovenous fistulas are congenital hemangiomatous malformations of the pulmonary vascular bed. In recent years, a close relationship between capillary telangiectasia (Rendu-Osler-Weber disease) and pulmonary arteriovenous fistulas has been recognized. In a series of 16 cases of pulmonary arteriovenous fistulas studied at The New York Hospital, 6 patients (38 per cent) had characteristic mucosal and skin lesions of Rendu-Osler-Weber disease.[1, 2] In addition, 2 patients in the series, although without capillary hemangioma, gave a history of such lesions in members of the family.

In 1952, a method of preparing metallic casts of anatomic specimens was described.[3] Essentially it consists of the pouring of a low melting point fusible metal into an anatomic specimen, allowing it to harden and then digesting the tissue with strong alkali. Pulmonary arteriovenous fistulas, being vascular malformations with afferent pulmonary arteries and efferent pulmonary veins, are admirably suited for such studies; particularly, because their gross anatomic features provide more information about the disease than does histologic study.[1] Since 1953, a total of seven excised pulmonary arteriovenous fistulas, three segmental and four lobar, were studied after casting. Six of the cases with casts of the operative specimen were previously reported[1, 2, 4]; the sixteenth patient with a pulmonary arteriovenous fistula and the seventh, with study of the specimen after casting, had disabling epistaxis due to nasal capillary telangiectases and is herein recorded.

CASE REPORT

A 46-year-old butcher (N. Y. H. No. 762570) was admitted to the hospital on March 17, 1957, with chief complaint of nosebleeds. Ever since childhood the patient had had epistaxis. At first these occurred about once a month but in the past year they had

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become more frequent, usually being associated with the loss of "about a cup" of blood. Packing and cautery of the nose had abated the bleeding at first but, recently, these measures had failed.

Seventeen years prior to admission, the patient had had a routine roentgenogram of the chest after enlistment in the National Guard, and when a "spot" was found in the right lung, the military service was terminated. Since then frequent x-ray studies of the chest had been made and the lesion had remained unchanged. At one time exploratory thoracotomy had been recommended but had been declined by the patient because symptoms referable to the respiratory system were absent. The patient's father had died at the age of 86 years, cause unknown. His mother, age 74 years, was still alive and she, 5 siblings, and several cousins had had epistaxis.

On physical examination the patient was pale, well developed and nourished. There was no cyanosis or clubbing of the fingers. Scattered small clusters of cherry red angiomata were seen over the face and trunk. The nose contained crusted blood and capillary angiomata; a few (less than 1 mm.) capillary angiomata were present over the nose and cheeks. The tongue (Fig. 1) also contained many angiomata. The blood pressure was 150/80 mm. Hg; the heart was regular and there were no murmurs. A loud systolic bruit was heard at the lower end of the right anterior chest; otherwise, the examination was normal.

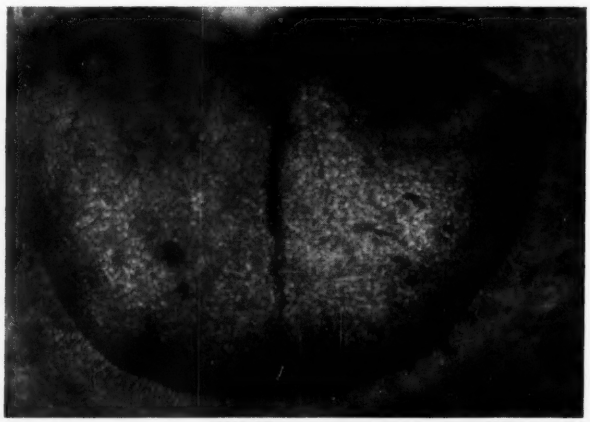

Fig. 1.—Photograph showing scattered capillary hemangiomata of the tongue characteristic of Rendu-Osler-Weber disease.

Laboratory data revealed secondary anemia with hemoglobin 9.8 Gm. per 100 c.c.; hematocrit, 29 per cent; bleeding and clotting times were normal. A roentgenogram of the chest (Fig. 2) showed a normal-sized heart. An oval 4.5 by 2.5 cm. mass with intimate relations to the vascular structures of the right hilus was seen at the right base. The lateral view (Fig. 2*B*) localized the lesion in the anterior segment of the right lower lobe. Angiocardiography (Fig. 3) clearly established the diagnosis of pulmonary arteriovenous fistula involving the anterior basilar segment of the right lower lobe. Treatment of the hemangiomata of the nasal mucous membrane by cauterization was followed by cessation of epistaxis. After transfusion, on March 22, 1957, segmental resection of the anterior segment of the right lower lobe containing the arteriovenous fistula was performed. A low melting point alloy cast of the specimen was made (Fig. 4). The patient was improved, and was discharged on March 31, 1957. Since then, recurrence of epistaxis, despite treatment with testosterone, packing, and x-radiation to the nasal mucosa, resulted in readmissions on April 9 and May 13, 1957.

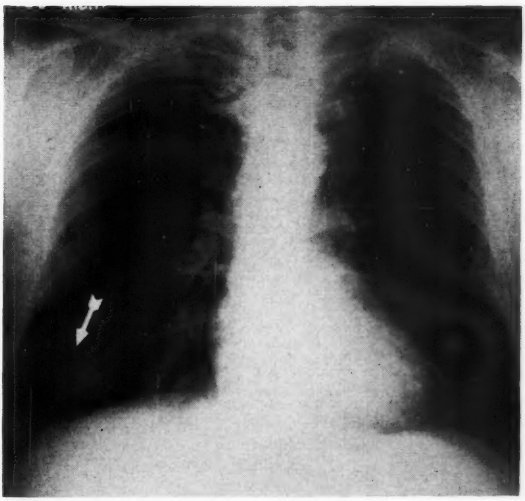

Fig. 2A.—Conventional frontal teleoroentgenogram of the chest showing a globular mass (arrow) with hilar vascular connection in the outer portion of the right lung.

Fig. 2B.—Lateral roentgenogram locates the lesion to be in the anterior segment of the right lower lobe (arrow).

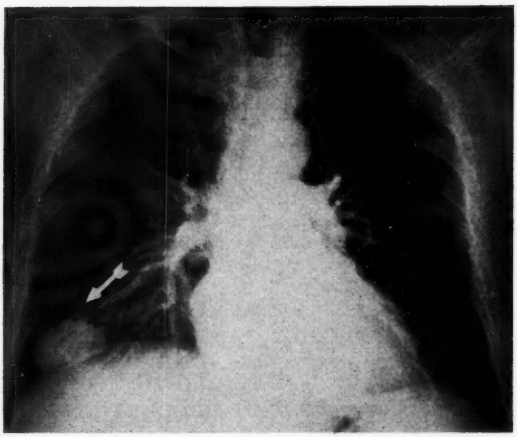

Fig. 3*A*.—Frontal teleoangiocardiogram, made 2½ seconds after the beginning of injection, reveals the afferent pulmonary arterial blood supply to the fistula (arrow).

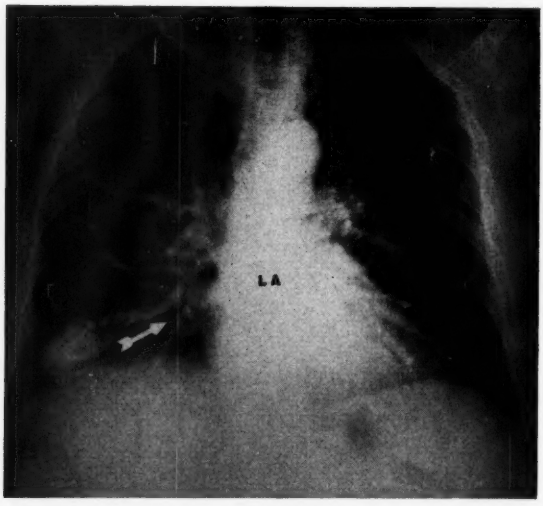

Fig. 3*B*.—At 5½ seconds, segmental pulmonary veins can be seen draining into the left atrium (*LA*).

COMMENT

Excision of a pulmonary arteriovenous fistula, once the diagnosis is established, is advisable even in the absence of respiratory complaints. This is because of the high incidence of brain abscess, cerebral thrombosis, and fatal hemoptysis in such patients. The risk from complications is far greater than the mortality and morbidity of lobectomy or segmental lung resection.[1, 2]

A glance at the cast of the pulmonary arteriovenous fistula made from the excised segment of the right lower lobe readily reveals the complexity of such lesions (see Fig. 4). Pulmonary arteriovenous fistulas are not merely communications between an afferent end pulmonary artery and vein. Rather,

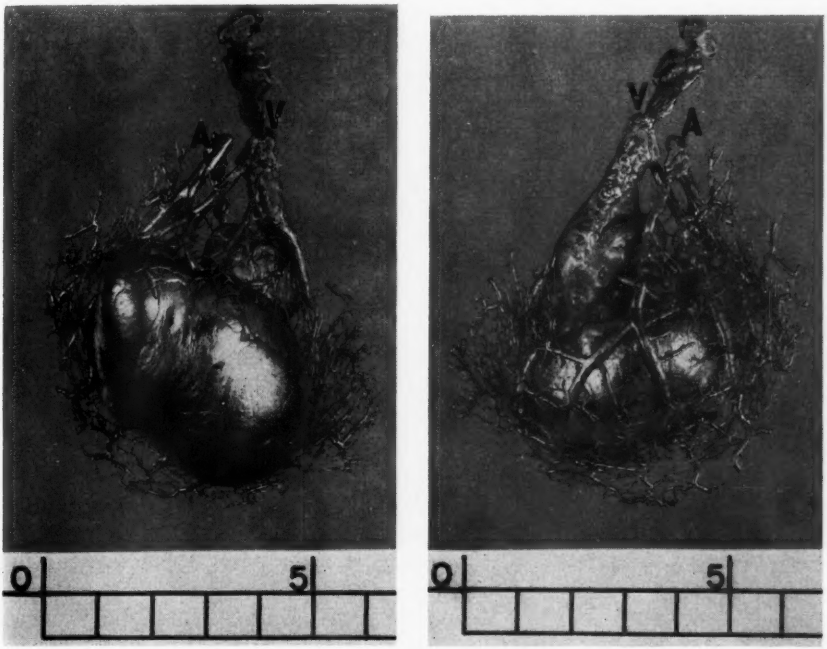

Fig. 4.—Alloy cast of pulmonary arteriovenous fistula. *Left*, Anteroposterior view. *Right*, Posteroanterior view. *A* is the pulmonary artery; *V*, the vein.

they are intricate lesions with centrally dilated paper-thin globular connections that frequently involve the entire blood supply of the lobe or segment. In addition, arterial and venous communications from neighboring chest wall, bronchus, or lung may occur. Indeed, the rich admixture of oxygenated blood from the bronchial arteries or pulmonary veins may prevent development of cyanosis.[1, 2]

Normally, the intact pulmonary capillary bed acts as a sieve and noxious agents, especially bacterial, are prevented from reaching the systemic blood supply. In the presence of right-to-left shunting of blood that occurs with

pulmonary arteriovenous fistulas, septic emboli may readily reach organs like the brain. A recent report of a liver abscess in a patient with a pulmonary arteriovenous fistula indicates that other organs may also be the sites of abscesses.[4]

SUMMARY AND CONCLUSION

Angiocardiography established the diagnosis of a pulmonary arteriovenous fistula of the right lower lobe in a 46-year-old man with epistaxis due to capillary telangiectases (Rendu-Osler-Weber disease). Segmental excision of the fistula and study of the specimen by making a metallic cast disclosed that fistulas are complex and bizarre hemangiomatous malformations.

Excision of pulmonary arteriovenous fistulas is recommended because, when they are removed, isolation of noxious agents in the pulmonary capillary bed prevents cerebral abscesses and thrombosis. The right-to-left shunting of blood is also corrected. Finally, since the fragile paper-thin fistulas have a tendency to rupture, removal will prevent fatal hemoptysis.

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SOME PROBLEMS IN EXTRAPLEURAL PNEUMONECTOMY FOR TUBERCULOUS EMPYEMA AND DESTROYED LUNG

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THE destroyed lung, due to tuberculosis complicated by empyema, has been an age-old problem. Estlander, in 1879, and Schede, in 1890, attacked the parietal portion of the empyema while Fowler and Delorme contributed to the visceral portion of empyema surgery. Experience gained during World War II marked another step in the surgical treatment of empyema; that of visceral decortication and early expansion of the underlying lung. More recently the combined procedure of excision of the empyema sac and the underlying diseased lung through the extrapleural plane has been the method of attack in these problems.[1] Contralateral pulmonary disease, decreased pulmonary function, resistance of the tubercle bacilli to antituberculous drugs, and the immeasurable immunologic status all contribute in the response of the patient to any given regimen of treatment. Those patients coming to extrapleural pneumonectomy and excision of the empyema "in toto" are a chosen few. On the other hand, many patients have been denied such definitive therapy because of complications arising during prolonged preparation or because of refusal to accept surgery.

A study of those patients undergoing pleuropneumonectomy as definitive therapy was undertaken. This paper is directed (1) to evaluate whether the extensive operative procedure of pleuropneumonectomy in complicated pulmonary tuberculosis yielded a sufficient number of rehabilitated patients, and (2) to examine the causes of complications in an endeavor to reduce the operative and late morbidity and mortality. Decortication and subtotal pulmonary resection will be discussed in another paper.

Both far-advanced pulmonary tuberculosis and tuberculous empyema carry a high mortality rate. This mortality rate is further increased by the presence of bronchopleural fistula and mixed empyema. Alling and co-workers,[2] in a study of far-advanced pulmonary tuberculosis in the prechemotherapy era, arrived at a figure of 70 per cent mortality in a 10-year follow-up, with 20 per cent mortality in the first year. Empyema without extensive pulmonary disease also carries a high mortality rate of 67.6 per cent within 5 years after the onset of empyema and a recovery rate of only 19 per cent.[3] Klassen and associates[4] reported a mortality rate of 38 per cent in empyema treated by thoracoplasty.

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Connolly and Forsee[5] reported a mortality of 18 per cent in pulmonary tuberculosis and empyema treated with thoracoplasty and streptomycin. These figures illustrate the gravity of active pulmonary disease complicated by empyema.

MATERIAL

From 1948 to December, 1955, 44 patients had extrapleural pneumonectomy performed for destroyed lung. Of these, 30 had chronic mixed empyema and bronchopleural fistula. Cases of acute empyema present an entirely different problem and are therefore excluded from this study. Fourteen patients had pleural symphysis from prior pleuritis or effusions, and a complete extrapleural procedure was necessary for the pneumonectomy. These cases are not included in the study. All except one patient had demonstrable contralateral disease.

Eighteen patients were prepared for pleuropneumonectomy by lesser surgical procedures such as closed thoracotomy, open thoracotomy or both, and 6 patients had thoracoplasty and 2 had further stages of Schede thoracoplasty. Since these procedures failed to obliterate the chronic empyema space and control the pulmonary disease, extrapleural pneumonectomy had to be performed. The mean length of preparation was 3 years.

COMPLICATIONS

The complication rate of pleuropneumonectomy, in comparison with other types of lesser pulmonary surgery in this series, was high. As a rule, patients undergoing this type of surgery do not represent the best surgical candidates.

The most serious complications were empyema, bronchopleural fistula, tuberculous spread to contralateral lung, distant spread of tuberculosis, and wound infection. Postoperative empyema developed in 17 of the 30 patients and 9 of these were demonstrated to have bronchopleural fistula. Contamination of the operative field by opening into the empyema was a definite factor in the development of postoperative empyema. Of 15 patients having operative contamination, 10 developed postoperative empyema. Seven patients developed spread to the contralateral lung or to distant areas and all of these cases were associated with the development of postoperative bronchopleural fistula and empyema.

Of the 17 patients who had postoperative empyema, 7 demonstrated drug resistance. Only 2 patients who had drug resistance did not have postoperative complications.

The following case reports illustrate some of the problems of the surgical procedure.

CASE 1.—F. F., a 29-year-old, acutely ill, Negro man, was admitted, in 1951, with extensive pulmonary tuberculosis of the right lung complicated with empyema and bronchopleural fistula. Minimal contralateral disease was present (Fig. 1). He was treated with closed thoracotomy drainage. After 50 days of streptomycin and PAS therapy, a right extrapleural pneumonectomy was performed on March 20, 1951. The postoperative course was uneventful and he was discharged from the hospital with a diagnosis of inactive tuberculosis. Follow-up roentgenogram (Fig. 2) demonstrates the status of the remaining lung.

Comment: This case illustrates the points that preliminary closed thoracotomy drainage does not necessarily lead to infection of the operative hemithorax and that protection against contralateral spread can be obtained by closed thoracotomy. A short course of preoperative drug therapy in stable disease was sufficient.

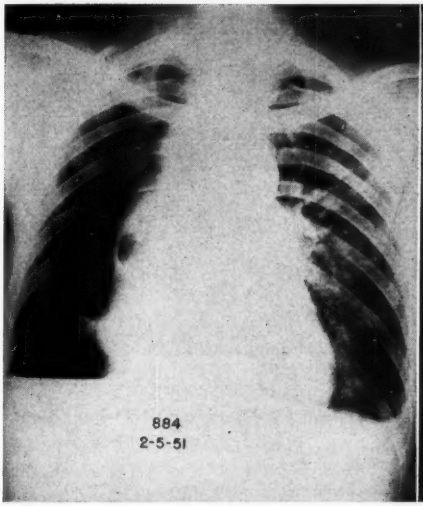

Fig. 1.

Fig. 2.

Fig. 1.—Case 1. Admission film shows empyema, bronchopleural fistula, and cavitary pulmonary disease. There is scattered disease on the left side.

Fig. 2.—Case 1. Postoperative film showing clear left lung field and right pneumonectomy 5 years postoperative.

CASE 2.—C. S., a 29-year-old white man, was admitted to the hospital in 1949 with pulmonary tuberculosis and right pneumothorax. After 4 months of drug therapy he left the hospital against medical advice. He was readmitted in 1950 with tuberculous empyema and bronchopleural fistula (Fig. 3). After one week of streptomycin therapy an extrapleural pneumonectomy was performed on June 29, 1950. Gross pleural contamination of the pleural space occurred during the operative procedure. Postoperative bronchopleural fistula and empyema ensued and a three-stage space-obliterating thoracoplasty was performed. The patient was discharged 28 months after surgery. Follow-up roentgenogram demonstrates stable disease in the remaining left lung (Fig. 4). The patient is now working.

Comment: This case illustrates the following classical points. Spontaneous pneumothorax in a tuberculous patient may lead to empyema and bronchopleural fistula. Inadequate preoperative drug therapy, operation on unstable disease, and operative pleural contamination can lead to major postoperative complications. Established long-term drug regimens and adequate preoperative stabilization of pulmonary disease can prevent many of the complications. Postpneumonectomy empyema and bronchopleural fistula necessitate major collapse therapy and prolonged hospital care.

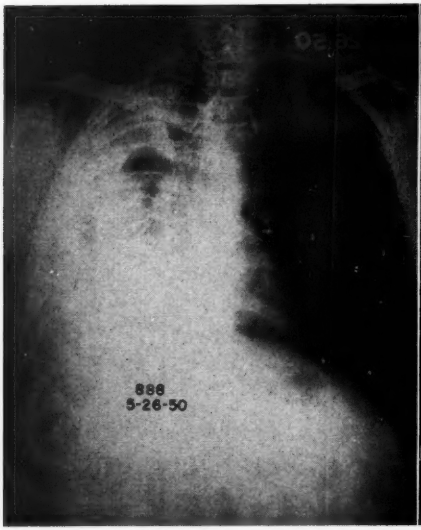

Fig. 3.

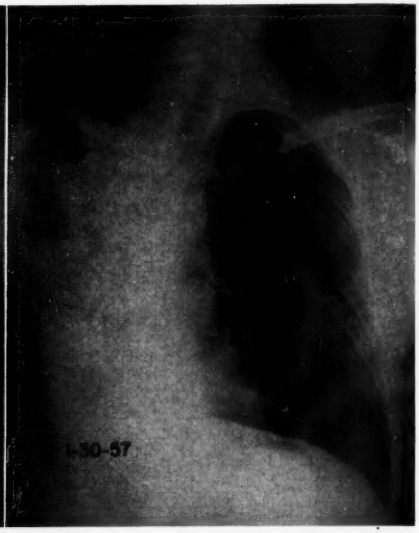

Fig. 4.

Fig. 3.—Case 2. Preoperative film shows right empyema, bronchiectasis and contracted lung.

Fig. 4.—Case 2. Follow-up film about 7 years after pleuropneumonectomy and thoracoplasty. Nodular but stable disease is seen.

Fig. 5.

Fig. 6.

Fig. 5.—Case 3. Admission film shows destroyed left lung, empyema, and bronchopleural fistula. Right lung contains moderately active disease.

Fig. 6.—Case 3. Follow-up film shows inactive disease 4 years after pleuropneumonectomy and thoracoplasty.

CASE 3.—G. B., a 38-year-old Negro man, with left fibrocavernous tuberculosis and bronchiectasis, complicated with empyema and bronchopleural fistula (Fig. 5), was initially treated with closed thoracotomy and later by open thoracotomy in 1948. Minimal contralateral disease was present at the time of admission. Subsequently, three stages of thoracoplasty and a Schede thoracoplasty failed to arrest the disease. Streptomycin, Promin and Tb I were administered from 1948 to 1950. On Aug. 2, 1952, under Aldenamide and PAS therapy, an extrapleural pneumonectomy was performed. The postoperative course was uneventful and he was discharged from the hospital in 1953. His present condition is excellent (Fig. 6). The disease is inactive and he is working.

Comment: In the face of contralateral disease, stabilization of the lesser lesion was obtained by drug therapy and bed rest. Reduction of the empyema space was obtained by thoracoplasty to prevent contralateral spread through the bronchopleural fistula. This was the accepted method of treatment prior to the development of antituberculous drugs.[6] The residual active pulmonary disease on a small empyema sac were finally successfully subjected to extrapleural pneumonectomy. This is an exceptional instance where an open thoracotomy wound did not result in an infection of the postoperative thoracic space.

CASE 4.—G. H., a 40-year-old Negro man, had had pulmonary tuberculosis since 1946 and had received right therapeutic pneumothorax for cavitary tuberculosis, resulting in chronic purulent empyema (Fig. 7). He was admitted to the hospital on July 23, 1948. After 6 weeks of bed rest, he was given 10 days of daily streptomycin and pleuropneumonectomy was performed on Sept. 20, 1948. Gross pleural contamination and an inadvertent opening of the pericardial sac occurred during the procedure. The postoperative course was complicated with pericarditis, empyema, bronchopleural fistula, and wound disruption (Fig. 8). The patient died 2 weeks postoperatively. Histologically, the resected lung showed tuberculous pneumonia.

Comment: The preoperative drug coverage in this patient was inadequate according to our present standards. An acutely ill patient should have closed thoracotomy drainage of the empyema. The exudative phase of the pulmonary lesion should be controlled before surgery. This reduces the number and attenuates the tubercle bacilli, permitting surgery in a less acutely inflamed field. With the newer multiple drug choices, in contrast to the available drugs of 1948, acute tuberculous postoperative complications have been prevented in the majority of instances.

CASE 5.—J. M., a 33-year-old white man, developed bronchopleural fistula and empyema following pneumonolysis in 1946. An open thoracotomy and two stages of posterolateral thoracoplasty were performed but the empyema and active parenchymal disease persisted (Fig. 9). In view of the known bacterial resistance, an extrapleural pneumonectomy was performed on Dec. 21, 1950, with no drug therapy. Postoperative contralateral spread developed and, 3 months later, a bronchopleural fistula was finally demonstrated. The patient died in irreversible pulmonary insufficiency and cor pulmonale 4 months after surgery (Fig. 10).

Comment: The undiagnosed postoperative bronchopleural fistula was a factor in contralateral spread and final demise of the patient. Bronchopleural fistula is the most common cause of postoperative spread of tuberculosis. Early diagnosis and empyema drainage may have obviated this mortality. Open

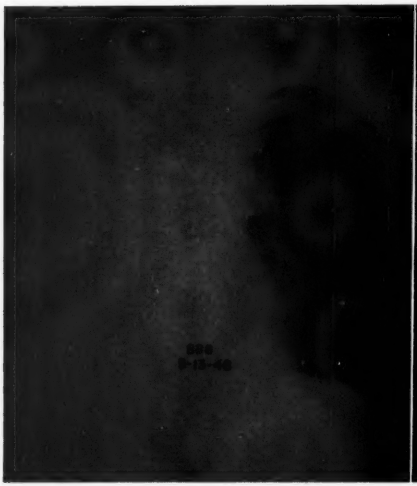

Fig. 7.

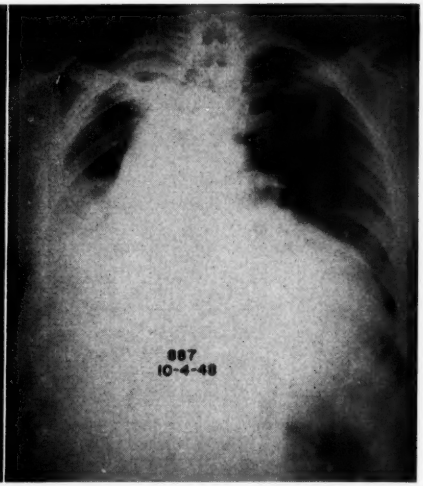

Fig. 8.

Fig. 7.—Case 4. Preoperative film showing right empyema. The pneumonic lesion under the empyema was not detected from x-ray examination. Examination of the resected specimen showed pneumonic disease.

Fig. 8.—Case 4. Postoperative film showing massive pericardial effusion, parascapular wound, and air-fluid level in the right chest.

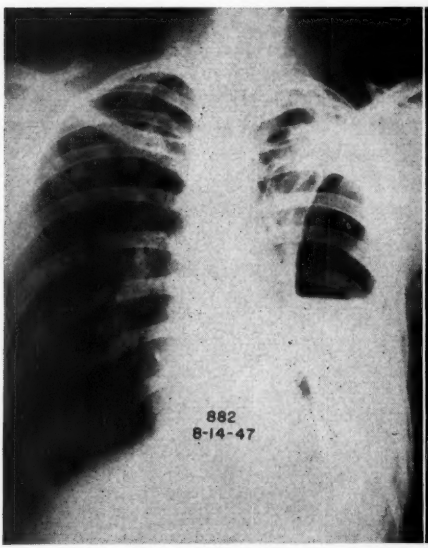

Fig. 9.

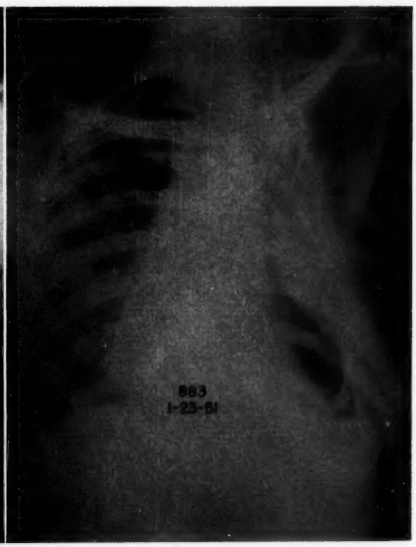

Fig. 10.

Fig. 9.—Case 5. Admission film shows left empyema and bronchopleural fistula and scattered lesions of the right lung.

Fig. 10.—Case 5. Postoperative film shows spread to right lung and empty left hemithorax due to bronchopleural fistula following pleuropneumonectomy.

thoracotomy preceding extrapleural pneumonectomy is almost always followed by infection of the thoracic space and therefore means of drainage should be established when pleuropneumonectomy is performed.

CASE 6.—E. W., a 36-year-old Negro man, was admitted to a state tuberculosis institution in 1954 with tuberculous empyema. He received streptomycin and isoniazid and had multiple chest aspirations. In March of 1956, he was transferred to VAH, Oteen, North Carolina. In July, a right decortication was performed. The operation was associated with excessive oozing from the raw surfaces, requiring 14,500 c.c. of blood before the operation was terminated. Postoperative bleeding continued and at re-exploration the chest was

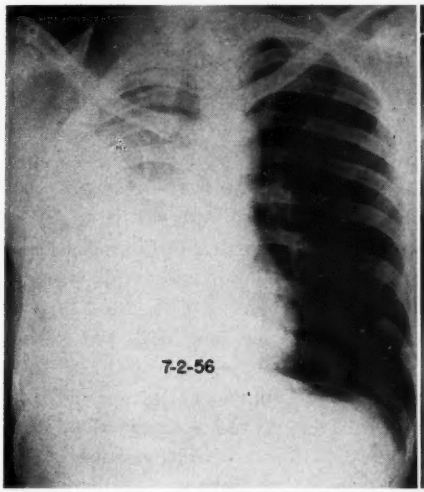

Fig. 11.

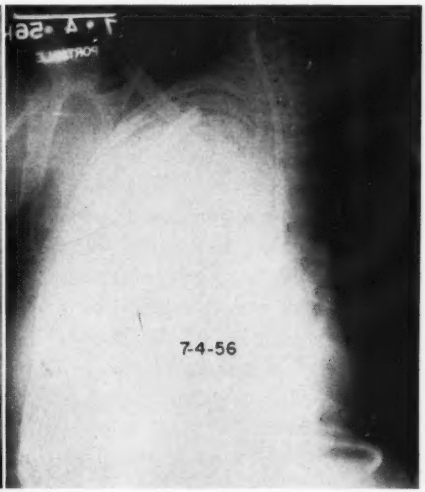

Fig. 12.

Fig. 11.—Case 6. Preoperative film shows right empyema and clear left lung.
Fig. 12.—Case 6. Postoperative film showing blood filled hemithorax with No. 34 Fr. catheters in place which were not adequate to evacuate the blood.

filled with clots; however, no bleeding points could be found. The lung was nonexpansible and there was bleeding through the endotracheal tube. An emergency pneumonectomy was performed. The patient continued to bleed postoperatively, and evidence of hypoxia was apparent. Blood transfusions and intermittent positive pressure breathing through an endotracheal tube did not relieve the situation. Fibrinogen determination, fibrinolysin level, blood volume, and prothrombin time were normal. The platelet count had dropped to 85,000 per cubic millimeter. The patient died 24 hours after the second thoracotomy.

Comment: Postoperative hemorrhage in major thoracic procedures is not an uncommon complication. Bleeding may be from open vessels which can be mechanically controlled; however, in oozing problems of various known and unknown causes, therapy becomes more difficult. Citrate excess, calcium deficiency, prothrombin deficiency or deficient prothrombin regeneration, fibrinogen deficiency or increased fibrinolysin titer, platelet deficiency, hypoxia, etc., as probable causes are all under study in various laboratories. Perhaps, in the near future, simple laboratory methods to determine the defects of clotting or bleeding and substitution therapy may become available to assist in the control of unexplained hemorrhage during and after major thoracic operations.

RESULTS

A follow-up study of 30 patients with chronic purulent tuberculous empyema treated with pneumonectomy and total pleurectomy was carried out. The follow-up period extended from 9 years to 14 months. Nineteen, or 63 per cent, of the patients have attained a diagnosis of inactive tuberculosis and are rehabilitated in proportion to the motivation of the patient. Three patients are cripples and still have active disease. Eight patients, or 27 per cent, have died from the following causes: meningitis, pericarditis, postoperative sepsis, contralateral spread resulting in pulmonary insufficiency and postoperative hemorrhage.

SUMMARY AND CONCLUSIONS

1. Thirty patients who underwent extrapleural pneumonectomy for chronic purulent empyema and destroyed lung were analyzed as to complications and final results. Representative cases are presented.

2. Adequate antituberculous drug coverage and stabilization of the pulmonary disease are necessary prerequisites for this type of surgery.

3. Contamination of the operative hemithorax by opening into the empyema frequently leads to postoperative empyema and bronchopleural fistula. These complications can be reduced by adequate drug coverage.

4. Preparation of the acutely ill patient with empyema with the use of preliminary closed thoracotomy drainage has enabled proper stabilization of the disease. Pneumonectomy and excision of the empyema sac can be performed subsequent to this without incident. Open thoracotomy should be performed only when repeated and accurate closed intercostal drainage procedures have been inadequate to control the progress of pulmonary tuberculosis and empyema. If open thoracotomy is performed, the pleuropneumonectomy must be accompanied by a drainage procedure.

5. If the empyema has been chronic and the pulmonary disease stable for several months, a long period of drug therapy is not necessary.

6. In the presence of bronchopleural fistula with empyema, operative intervention should be done early in the course before the development of contralateral spread and drug resistance. If the general condition of the patient is unsatisfactory for major resection, complications can be prevented by space-obliterating thoracoplasty. Pleuropneumonectomy can then be performed in a less infectious field at a later date.

7. Postpneumonectomy bronchopleural fistula is the most common cause of postoperative contralateral pulmonary spread. The patient with postoperative spread should have careful examinations for determining the presence of bronchopleural fistula.

8. Two thirds, or 63 per cent, of the patients having chronic purulent tuberculous empyema and destroyed lung have obtained an inactive diagnosis and have been rehabilitated following extrapleural pneumonectomy. These patients were judged by the surgical staff as not being curable by other lesser

operative procedures. Some had prior thoracoplasty. Pleuropneumonectomy, although a procedure accompanied by high complication rate, is a useful procedure for patients having no other recourse.

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EFFECT OF INFLOW OBSTRUCTION AND RAPID BLEEDING ON VENTRICULAR DIASTOLIC PRESSURE

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BLOOM and Ferris,[1, 2] studying the excised beating rat heart immersed in liquid, demonstrated the development of negative left ventricular pressure during diastolic ventricular filling by suction. These authors[1] also found negative diastolic pressure in the right and left ventricles of the dog when inflow to the ventricle was obstructed. Brecher[3] demonstrated that the left ventricle of the dog was capable of exerting a sucking effect when its inflow was blocked. Kraner and Ogden[4] showed that the ventricle of the turtle was capable of exerting diastolic suction. The purposes of the present study were as follows: (1) to confirm and extend the above observations on the frequency and degree of negative ventricular diastolic pressure developed when there is obstruction to inflow; (2) to ascertain whether the magnitude of negative ventricular diastolic pressure developed during obstruction to inflow is influenced by infusion of l-norepinephrine; and (3) to determine whether negative ventricular diastolic pressure develops during diminution of ventricular filling as a result of acute hemorrhagic hypovolemia.

PROCEDURE

The studies to be described were performed upon 20 mongrel dogs, anesthetized with pentobarbital sodium, 30 mg. per kilogram of body weight. Studies were made with the animal on its back, the chest open, and with positive pressure respiration. Right and left ventricular pressures were measured through a No. 12 cannula with side perforations near the tip. The tricuspid valve was used as a zero reference level. Pressures were detected by means of a Statham P23Da strain gauge and were recorded upon a Sanborn Poly-Viso Electrocardiograph or upon an Electronics for Medicine Research Recorder. Diastolic pressures were recorded at the nadir of diastole. Paper speeds were 5 to 25 mm. per second. Right ventricular pressures were recorded at a sensitivity of 40 mm. Hg per 4 cm. paper; left ventricular pressures were recorded

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at a sensitivity of 100 or 200 mm. Hg per 4 cm. paper. Records were checked for electrical drift before and after each run. Pressure transducers were calibrated with a mercury manometer before and after each experiment.

Left ventricular pressures of the open chest dog were measured before, during, and after obstruction to inflow. Inflow obstruction was produced by inflation of the bag of a Foley catheter inserted through the left auricular appendage. The tip of the catheter lay in the left ventricle, and the bag itself lay inside the mitral ring. The bag was inflated with 40 to 55 c.c. saline to produce inflow blockage. It was planned to record pressures before, during, and following obstruction on three occasions for each animal. In 9 animals, left ventricular pressures during obstruction were measured also during infusion of l-norepinephrine in an amount sufficient to increase left ventricular systolic pressure by approximately 50 to 100 per cent. Right ventricular pressures were measured before, during, and after obstruction to filling produced by occlusion of the superior vena cava, inferior vena cava, and coronary sinus. In some animals, left ventricular pressure was measured during rapid exsanguination through a rubber tube inserted through the wall of the right ventricle. Pressures recorded during obstruction to inflow or bleeding represent an average of several heartbeats after reaching a maximal negative pressure at a fairly steady level.

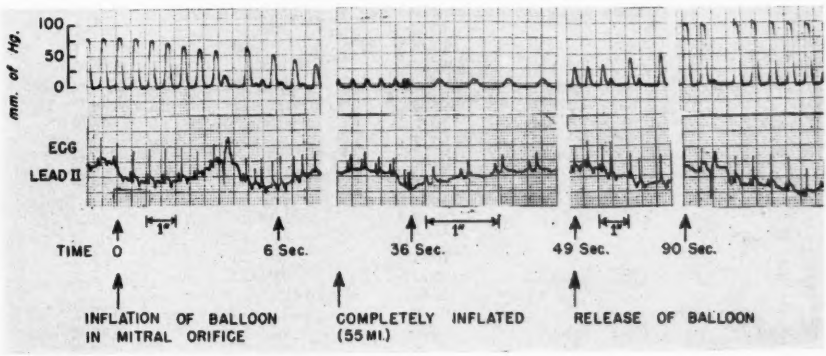

Fig. 1.—Record of left ventricular pressure during obstruction to inflow by inflation of left atrial balloon. Pressure is 80/0 mm. Hg before obstruction and 8/–5 mm. Hg during maximal effect. Pressure is 95/0 mm. Hg after deflation of balloon. Paper speed is accelerated from 10 to 25 mm./sec. during maximum effect.

RESULTS

Results are given in Tables I to III and in Figs. 1 to 3. Satisfactory records of left ventricular pressure during obstruction to inflow (Table I) were obtained on 32 occasions in 13 animals. Adequate records of left ventricular pressure during l-norepinephrine infusion and inflow obstruction were obtained in 18 runs on 9 animals. The results are given in chronological sequence for each animal. It may be seen that control diastolic pressures were

TABLE I. EFFECT OF OBSTRUCTION TO INFLOW UPON LEFT VENTRICULAR PRESSURE, MM. HG

DOG	BEFORE OBSTRUCTION	DURING OBSTRUCTION	FOLLOWING OBSTRUCTION
1-11-57	92/5	10/–3.5	86/5.5
	95/3	7/–5.5	73/3.5
	86/1.5	8/–3.5	93/3
(N.E. inf.)*	138*/0	48/–8.5	138*/6
1-18-57	63/1.5	17/–3	73/1.5
	50/0	13/–5	73/3
1-25-57	116/6	–5/–10	118/2.5
	116/3	10/–5	115/7.5
(N.E. inf.)	165/4	–10/–20	185/0
(N.E. inf.)	168/8.5	14/–6	150/8
(N.E. inf.)	167/6.5	9/–6	170/15
	110/0	15/–8	105/0
2-15-57	115/1.5	20/–2.5	150/2.5
	124/6.5	15/–5	130/2.5
2-22-57	64/3.5	9/–2	--
	104/1.5	5/–3.5	88/3.5
(N.E. inf.)	150/3.5	23/–10	103/6.5
	106/3.5	20/–18	96/3.5
(N.E. inf.)	146/1.5	6/–17	152*/4.5
3- 8-57	117/0	24/–4	125/3
3-22-57	126/2.5	10/–5	130/6
	126/6	9/–5	155/9
(N.E. inf.)	205/8	25/–5	--
3-22-57 (N.E. inf.)	205/4	13/–9	--
	90/4	15/–3.5	115/4
	130/7.5	18/–3.5	118/4
4- 5-57	135/7.5	14/–5	180/10
	125/4	10/–5	157/5
(N.E. inf.)	200/2.5	15/–5	--
4-12-57	113/5	10/–9	115/2.5
	115/2.5	0/–10	108/1.5
(N.E. inf.)	200*/0	15/–10	200*/0
(N.E. inf.)	200*/2.5	20/–10	200*/2.5
(N.E. inf.)	240/5	23/–10	240/5
	110/2.5	9/–6	105/2.5
	105/1	10/–5	105/2.5
5- 6-57	91/3	8/–2.5	103/5
	88/4	9/–2.5	80/3
(N.E. inf.)	140/8	20/–5	--
(N.E. inf.)	145/1.5	30/–3	--
5- 8-57	70/2.5	–1/–3	60/5
No. 1	73/1	16/–2.5	74/1
(N.E. inf.)	120/1.5	21/–2.5	--
	115/2.5	22/–2.5	--
5-9 -57	105/2.5	15/–4.5	150/2.5
5-10-57 (N.E. inf.)	125/0	15/–5	140/0
	88/2.5	12/–2.5	75/0
(N.E. inf.)	120/0	35/–4	170/5
	80/0	8/–5	95/0
(N.E. inf.)	150/1	13/–6	160/5

*Norepinephrine infusion.

from zero to 7.5 mm. Hg. During inflation of the left atrial balloon, negative left ventricular diastolic pressure was observed in each instance, pressures ranging from –2.5 to –18 mm. Hg. Following release of the obstruction, left ventricular diastolic pressure became atmospheric or positive in each instance, ranging from zero to 10 mm. Hg (Table I). Diastolic left ventricular pressures during l-norepinephrine infusion were zero to 8.5 mm. Hg. Upon obstructing inflow during l-norepinephrine infusion, left ventricular diastolic

pressures were –2.5 to –20 mm. Hg. In only 5 of 9 animals were the peak negative pressures during norepinephrine infusion greater than those without norepinephrine infusion. In 3 of these 5 animals, maximum negative pressures reached during inflow blockage were not consistently greater during l-norepinephrine infusion. In 3 runs on 2 animals, systolic pressures also became negative during obstruction to inflow. An example of the effect of obstruction to left ventricular inflow upon left ventricular pressure is given in Fig. 1.

Table II gives the effect of obstruction to right ventricular inflow upon right ventricular pressure in 11 runs on 5 animals. Before inflow occlusion, right ventricular diastolic pressures were zero to 1 mm. Hg; during obstruction to right ventricular inflow, negative diastolic pressure was observed in each instance, the pressures ranging from –1 to –2.6 mm. Hg. Following the release of obstruction to inflow, right ventricular diastolic pressure became positive in each instance, ranging from 0.8 to 2 mm. Hg. An example of the effect of inflow occlusion upon right ventricular pressure is shown in Fig. 2.

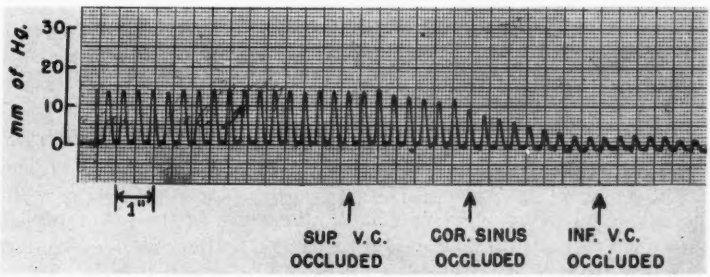

Fig. 2.—Record of right ventricular pressure during obstruction to inflow produced by occlusion of coronary sinus, and superior and inferior venae cavae. Pressure is 14/1 mm. Hg before obstruction, and 2/–1 mm. Hg during obstruction.

Table II. Right Ventricular Pressures, mm. Hg, During Obstruction of Inflow

Dog	Before Obstruction	During Obstruction	Following Obstruction
5-6-57	17/0.8	1.2/–1	24/1
	20/1	2/–1	22/2
	22/1	1/–1	24/1.5
5-8-57	32/0	0/–1.8	26/1
No. 1	25/0.6	2/–1.2	27/1
5-8-57	23/1.2	4/–1	24/0.8
No. 2	23/0.6	4/–1.2	26/1.6
5-9-57	19/0.2	–1/–2.6	25/0.8
5-10-57	20/1	–1/–2	31/1
	14/1	0/–2	14/1
	13/0.4	0/–2	16/1

The effect of rapid bleeding upon left ventricular pressure is given in Table III. The volumes of blood removed were from 360 to 700 c.c., and the time required for bleeding was 89 to 236 seconds. Control left ventricular diastolic pressures were zero to 5 mm. Hg. During bleeding, maximum negative diastolic pressures were –2.5 to –6.5 mm. Hg. Negative diastolic pressures

appeared as early as after removal of 100 c.c. of blood, or as late as after removal of 400 c.c. of blood. In some instances, the maximum negativity declined toward the end of the bleeding period. An example of the effect of bleeding on left ventricular pressure is shown in Fig. 3.

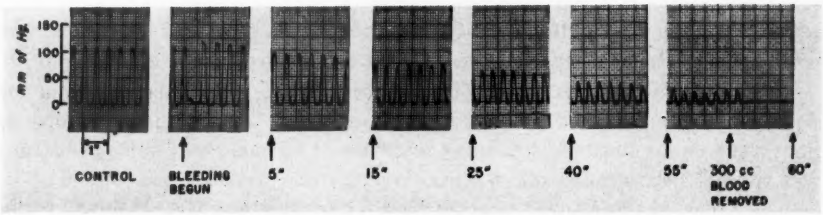

Fig. 3.—Record of left ventricular pressure during rapid bleeding from the right ventricle. Pressure is 110/0 mm. Hg at onset of bleeding and 20/−5 mm. Hg after removal of 300 c.c. blood. Horizontal tracing at end of record represents check for electrical drift.

TABLE III. EFFECT OF EXSANGUINATION UPON LEFT VENTRICULAR PRESSURES, MM. HG

	BEFORE EXSANGUINATION	DURING EXSANGUINATION
DOG	PRESSURE	LOWEST DIASTOLIC PRESSURE
2-12-57	105/0	5/−6.5
2-22-57	137/3	8/−3.5
3-22-57	125/4	2.5/−5
5- 6-57	80/5	10/−6
5-10-57	60/0.5	8/−2.5

DISCUSSION

The development of negative diastolic pressure in the left ventricle during acute obstruction to inflow was a consistent finding, and confirms the observations of previous investigators.[1, 2, 3] When obstruction to inflow was produced during l-norepinephrine infusion, there was an increase in the amount of negative left ventricular diastolic pressure in some but not in all observations. These observations were similar to those of Brecher[3] after epinephrine, which was followed by increased negative ventricular diastolic pressure during inflow obstruction in some but not in all instances. If l-norepinephrine infusion decreases the volume of blood in the heart, then greater negative pressure in diastole may be expected, as shown by the studies of Brecher and Kissen,[5] who found increasing degrees of negative pressure when ventricular volume was decreased below a certain critical level. The interference with the circulation of l-norepinephrine to the myocardium during the period of occlusion of inflow may account for our failure to observe consistent increases in ventricular diastolic negative pressure during l-norepinephrine infusion. As observed by Brecher,[3] negative ventricular diastolic pressure did not develop immediately upon obstruction to filling, but rather after several heartbeats. This suggests that negative pressure is evidenced only after the heart has reduced itself to a critical volume by expulsion of its contents in systole.

The development of negative pressure in the right ventricle during occlusion to inflow was also consistent, although the number of animals studied

was small. The magnitude of negative pressure developed was much less than in the left ventricle, which could be attributed to differences in pressure-volume curves of the two ventricles, or to less complete emptying of the right ventricle upon inflow occlusion. Brecher and Kissen[5] demonstrated that the sucking force of the left ventricle of the dog's heart was greater than that of the right ventricle.

The development of negative diastolic pressure in the left ventricle during rapid bleeding is of interest. Although the importance of ventricular suction in ventricular filling in the normal circulation has not been proved, this observation suggests that ventricular suction may be important in ventricular filling during states of acute hypovolemia. The measurement of ventricular volume under these circumstances would be of interest, since in the active circulation, negative diastolic pressure may develop at a higher ventricular volume than was found by Brecher and Kissen in their study[5] upon the dog's heart in standstill.

SUMMARY

A study was made of the effect of obstruction to inflow upon diastolic pressure in the left and right ventricles in dogs. The effect of rapid bleeding upon left ventricular diastolic pressure was also observed. During obstruction of the mitral valve orifice, negative pressure of −2.5 to −18 mm. Hg was observed in the left ventricle. In the right ventricle, diastolic pressure during obstruction to inflow was −1 to −2.6 mm. Hg. During acute bleeding, diastolic pressure in the left ventricle became negative, with maximum values being −2.5 to −6.5 mm. Hg.

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PULMONARY ASPERGILLOMA

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CASES of pulmonary aspergillosis have been described intermittently in medical literature since the original description by Virchow[1] in 1856. He demonstrated the pathogenicity of aspergilli in the pigeon feeders of Paris, who masticated grain and then force-fed the birds. It was also described in wigmakers who employed corn meal to clean wigs. In both instances the grain was said to be the source of the mold.

Yesner and Hurwitz[1] have differentiated three forms of aspergillus pulmonary infection in man: (1) the severe pneumonic type characterized by acute pneumonia, and generalized aspergillosis which is usually fatal; (2) a mild form characterized by an acute tracheobronchitis, which runs a benign course; and (3) chronic forms which resemble tuberculosis, often with cavitation or chronic granulomas. These authors reported a case treated by left lower lobectomy in which there was a cavity, 4 by 2.5 cm. in size. Organisms were cultured from the walls of the cavity.

Pesle and Monod[2] described 3 patients who were operated upon for "aspergilloma." In 2 patients, cavity drainage was established with one death, and in one instance a successful segmental resection was performed. The lesions in these patients were similar and characteristic in that they had the appearance of a cavity, not entirely filled, in which the central opaque material surrounded by a crescent of air. The lung surrounding this lesion is usually normal.

A recent study by Vellios and associates[6] includes a case report of a patient with an "aspergilloma," in whom the radiologic and pathologic features were typical. These authors succeeded in finding 22 previously reported similar cases. They set forth a theory of origin of these lesions, which we had postulated independently that these masses occur in previously existing pulmonary lesions, such as congenital cysts, areas of bronchiectasis, old tuberculous cavities, or cavities of pyogenic origin.

The following case is presented because of the characteristic roentgen appearance which made the diagnosis immediately apparent, and because the patient had an extraocular sixth nerve palsy, causing diplopia which subsided shortly after resection of the pulmonary lesion.

CASE REPORT

Mrs. G. M., aged 52, was admitted to Milwaukee Hospital on Aug. 6, 1956, and discharged on Sept. 6, 1956. In May, 1956, she noted double vision on two occasions. The diplopia was

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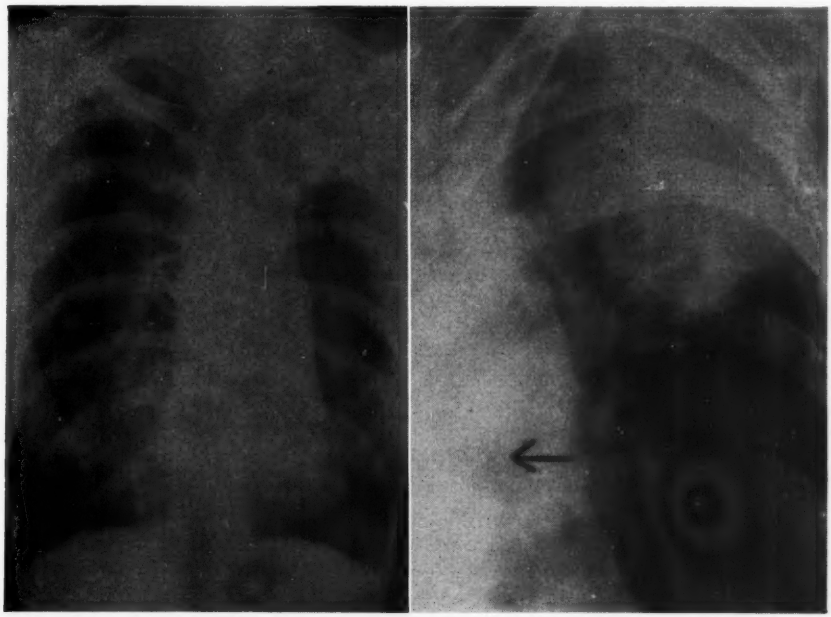
of short duration, usually only several hours, and subsided spontaneously. In June, 1956, the diplopia recurred and persisted. She consulted an ophthalmologist who diagnosed an extraocular muscle paresis with strabismus. The optic fundi were normal. A complete study elsewhere, including roentgenograms of the skull and gastrointestinal tract, was negative except for a "mass in the left upper lobe of the lung." Neurologic examination showed only one internal strabismus, with normal spinal fluid. Bronchoscopy was reported negative. There were no symptoms referable to the chest.

Physical examination yielded only the following positive findings: the right pupil was slightly larger than the left; there was a slight internal strabismus of the right eye; the teeth were in very poor repair.



A. *B.*

Fig. 1.—*A*, Posteroanterior films of chest showing lesion of left upper lobe. *B*, Spot film of left apex showing appearance of air crescent with change of position of patient.

Laboratory studies showed a normal urine; white blood cells numbered 14,050 per c.c. of which 72 per cent more segmented neutrophils, and 14 per cent were lymphocytes. The NPN was 42 mg. per cent.

Bronchoscopy showed a normal tracheobronchial tree. A culture of material aspirated from the bronchi yielded a heavy growth of aspergillus. Gastric contents and sputum cultures were negative for tubercle bacilli.

Roentgenograms showed a normal heart and mediastinum with minimal calcified areas in the right apex interpreted as old healed calcified tuberculosis. There was an increased density in the left upper lobe which appeared to be a cavity almost completely filled with a solid homogeneous substance. This material appeared not to be fixed in place since it changed position in the upright and decubitus positions (Fig. 1). A diagnosis of aspergilloma was made by the radiologist since it resembled so closely the cases reported by Höffken[4] and Levin.[5] Culture of material aspirated from the bronchus corroborated this impression.

Left thoracotomy was performed on Aug. 9, 1956. A large thick-walled abscess, 6 cm. in diameter, occupied the apical and posterior segment of the upper lobe, involving also the superior portion of the fissure between it and the superior segment of the lower lobe. The abscess was densely adherent to the chest wall and ruptured while being freed. A large amount of greenish material was removed from the abscess cavity which the pathologist reported as containing "mycelia." Upper lobectomy was deemed advisable because of small abscesses in other portions of the upper lobe. The involved superior segment of the lower lobe was also resected. The thorax was thoroughly irrigated with normal saline solution because of the contamination resulting from rupture of the abscess.

Pathologic Report.—A cavity 6 cm. in diameter contained greenish curdled material. The walls of the cavity measured up to 5-6 mm. in thickness. Part of the cyst was lined with very rough hemorrhagic pulmonary tissue, partly by smooth white pulmonary tissue, and partly by smooth white membranous tissue. There was a patent bronchus 3 to 4 mm. in diameter communicating with the cavity. The remainder of the lobe contained one small abscess, and the bronchi showed bronchiectasis of moderate degree.

Microscopically, the cyst wall was lined by mature respiratory epithelium and in some places had undergone metaplasia to resemble squamous epithelium of the skin. There was plasma-cell infiltration and considerable fibrosis.

Aspergillus was again cultured from the amorphous mass in the cavity.

Postoperatively, one gram of streptomycin, and 400,000 units of penicillin were administered once daily for 6 days. Convalescence was uncomplicated. On the fourth postoperative day, the internal strabismus disappeared completely and has not recurred. There was minimal air leak from the raw area of lower lobe in the area of local resection for a period of one week. This sealed off spontaneously.

The patient was discharged from the hospital on Sept. 6, 1956. Examinations have been conducted at monthly intervals and they have been negative. Cultures of sputum and gastric aspirations have been negative for aspergillus and tubercle bacilli.

DISCUSSION

Höffken felt that the cavity in which the mold had grown in his patient represented a congenital cyst secondarily infected. Pesle (2) suggested that the disease occurred in a pre-existing cavity, probably of tuberculous origin. It appears likely that the cavity in the present case may have been tuberculous in origin, but this cannot be definitely proved since neither history, examination of the lung, nor bacteriologic studies of the sputum, bronchial, and gastric secretions yielded evidence of tuberculosis. The presence of bronchiectasis in the resected lobe raises the possibility that the original lesion was a bronchiectatic abscess which became secondarily infected by the fungus. It seems unlikely that the fungus was the causative agent of cavitation since this is unprecedented and uncharacteristic of the usual behavior of the organism.[6] The characteristic roentgenographic appearance of a solid homogeneous mass, lying free in a cavity and surrounded by a clear halo which shifted on the change of position of the patient, seems to be pathognomonic of this form of pulmonary aspergillosis. It is significant that the lesion occurred, as in all previous cases, in the upper lobe and superior segment of the lower lobe.[5]

The extraocular muscle paresis cannot be satisfactorily explained even on the basis of a toxic reaction to the organism, but symptoms referable to vision have not occurred since operation.

The source of infection in this patient is unknown. She has always been an urban dweller and has had no contact with grain or livestock. It may be

that the severe pyorrhea and dental sepsis may have been the source of the aspergillosis, but proof is lacking.

SUMMARY

A case of pulmonary aspergilloma is presented which was so similar in roentgenographic appearance to 7 previously reported cases that the diagnosis was made on roentgenograms of the chest alone, corroborated by bacteriologic studies.

Cure was effected by lobectomy and segmental resection.

A transient diplopia due to a right sixth nerve paresis, present for several months before operation, has not recurred since operation.

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PULMONARY ASPERGILLOSIS

A Case Report

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ASPERGILLOSIS may affect the lung as a primary or secondary infection. It may be secondary to tuberculosis, bronchiectasis, or other chronic lung diseases, and is commonly found in post-mortem material. However, primary pulmonary aspergillosis is not a common clinical entity. Reports are now beginning to appear in the literature which help to elucidate some frequent findings in this entity. It is only recently that pulmonary resection was undertaken for this lesion. As increased numbers of cases appear in the literature, a more thorough evaluation as to etiology, symptomatology, physical findings, roentgenograms, and therapy may be obtained. The case to be presented represents a patient with primary pulmonary aspergillosis who underwent surgical resection of the involved lobe of the lung, with apparent cure of his disease.

CASE REPORT

A 44-year-old married male furniture employee was hospitalized in January, 1956, for evaluation of painless hematuria. The first episode of hematuria had occurred 2 months previously and had been followed by several recurrences. A routine urologic evaluation was performed, including intravenous pyelograms, urine cultures, cystoscopy, and retrograde pyelograms. All studies were unremarkable except for a Class III Papanicolaou smear from the right ureter. Urine cultures were negative for acid-fast bacilli; bleeding, clotting, prothrombin time, and platelet counts were normal. Roentgen examination of the chest revealed a large cavity in the right apex measuring 5.0 by 5.5 cm. in diameter with a fluid level. An area of increased density surrounded the cavity and was interpreted as representing an active inflammatory process.

The patient was transferred to a sanatorium for further diagnostic studies. Five sputum examinations, 3 gastric lavages, and 3 urine specimens were all negative on direct smear and culture for acid-fast bacilli. Intradermal skin tests for tuberculosis, blastomycosis, coccidioidomycosis, and histoplasmosis were nonreactive. A bronchogram, using Dionosil, revealed no abnormalities; the contrast medium did not enter the cavity in the right apex.

The patient was readmitted to the hospital in February of 1956 for elective pulmonary surgery.

Past history included gonorrhea and syphilis infection, in 1931, treated with salvarsan; repeated urethral dilations for stricture; penicillin treatment on the basis of positive serum and spinal fluid Wassermann in 1947 and 1950; bismuth and tryparsamide therapy in 1948; duodenal ulcer with obstruction and subtotal gastrectomy in 1954.

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Physical Examination.—The blood pressure was 110/70 mm. Hg, pulse 80, and respirations 18. The patient was a well-developed but thin male. The pupils did not react to light, and were round and regular but unequal in size. The trachea was in the midline, and percussion and auscultation of the chest revealed no abnormalities. The remainder of the general physical examination was negative. Deep tendon reflexes in the lower extremities were absent.

Laboratory Data.—Urinalysis was negative except for microscopic hematuria. The hemogram was normal and serum chemical determinations, including blood urea nitrogen, total serum protein, albumin-globulin ratio, carbon dioxide combining power, chlorides, Bromsulphalein, and prothrombin time, were all within normal limits. Serologic test for syphilis was nonreactive. Roentgenographic examinations of the chest revealed the cavity to be decreased in size; however, a fluid level was still present. Electrocardiogram was normal.

Fig. 1.—Roentgenogram of chest of patient on admission to hospital. Large cavity in the right apex of lung.

Course.—An exploratory thoractomy was performed under endotracheal gas, oxygen, and ether anesthesia through the bed of the right fifth rib. Several thin adhesions binding the right upper lobe to the parietal pleura were divided without difficulty. The apex of the right upper lobe was firmly attached to the parietal pleura and this was dissected free. Grossly, the inflammatory process appeared to involve the major portion of the right upper lobe, as most of the lobe was noncrepitant. A right upper lobectomy was performed. The postoperative course was uneventful; the thoracotomy tubes were removed on the third postoperative day and the skin sutures were removed on the seventh postoperative day. There was good expansion of the right middle and lower lobes and wound healing was excellent. The patient has been followed in the clinic 18 months and no other evidence of pulmonary infection has been demonstrated. A urine culture was negative for Aspergillus. The postoperative course has been quite satisfactory and the patient has now returned to gainful employment.

Pathology.—

Gross: A lobe of a lung that weighed 200 Gm. The surface was gray, mottled black, and red, and a number of small blebs were present. On sectioning, a cavity measuring 3.0 cm. was seen near the hilus. The cavity was filled with yellow, soft material and the wall was 0.1 to 0.4 cm. in thickness. Adjacent to the large cavity were many smaller cavities that varied from 0.1 to 1.0 cm. Many of these were filled with yellow, soft material. The bronchus was slightly dilated but did not communicate with the cavities.

Microscopic: The lung contained numerous cavities that were lined by epithelioid cells, multinucleated giant cells, and fibrous tissue. In their centers were necrotic material, a large number of granulocytes, macrophages, and numerous branching hyphae. Similar hyphae were present in the wall, surrounded by multinucleated giant cells. These hyphae were periodic

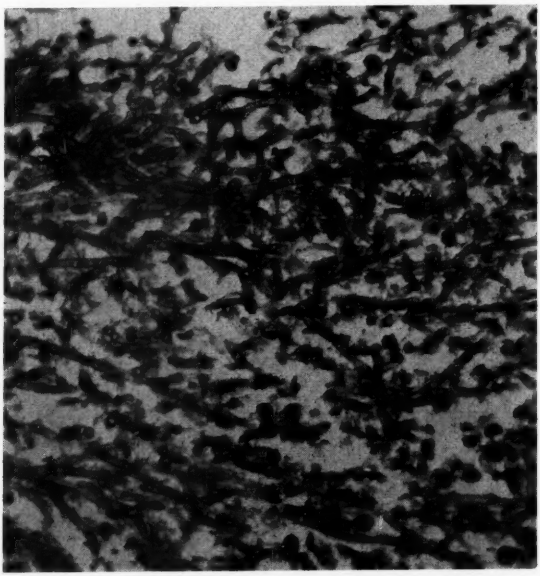

Fig. 2.—Photomicrograph of hyphae of aspergillus in center of large cavity in lung. (×480; reduced ⅙.)

acid-Schiff positive. In the surrounding lung tissue there was rather marked fibrosis as well as an increased number of lymphocytes. Areas of focal calcification as well as scattered macrophages containing brown pigment were present in the fibrous tissue. The bronchi and bronchioles were slightly dilated and contained lymphocytes and plasma cells in their walls.

Bacteriology: The resected lung was cultured and a pure culture of *Aspergillus fumigatus* Fresenius was obtained. The fungus was identified by Dr. Kenneth B. Raper, Department of Bacteriology, College of Agriculture, University of Wisconsin, Madison, Wisconsin.

Acid-fast cultures were negative for *Myocbacterium tuberculosis.*

DISCUSSION

Aspergillus is commonly found in nature and its spores frequently infest both plants and animals. Most of the cases of aspergillosis of the lungs in human beings have been due to the species *Aspergillus fumigatus.* This is the organism which was cultured from our patient. Conant and associates[1] state that the

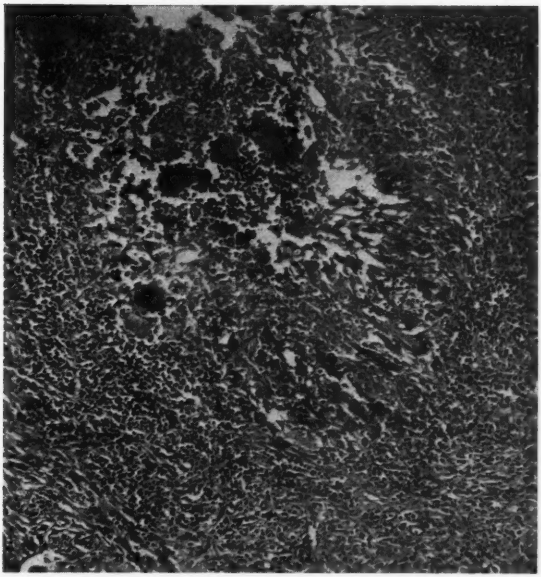

Fig. 3.—Photomicrograph of a granuloma in lung adjacent to a cavity. Giant cells, epithelioid cells, and granulocytes are present. (×142; reduced ⅙).

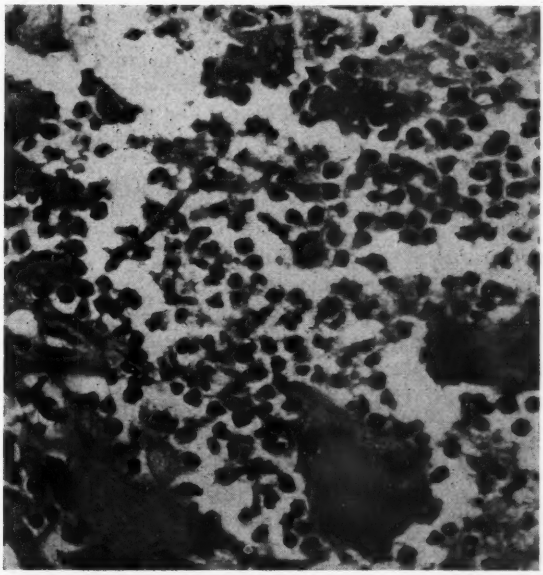

Fig. 4.—Higher magnification of Fig. 3. Note the hyphae of aspergillus and the giant cells. (×480; reduced ⅙.)

disease is commonly seen in the following workers: (1) squab feeders, (2) fur cleaners who use rye flour, and (3) agricultural workers exposed to dust from threshers. The patient under discussion was a furniture worker.

Earlier writers on the subject of aspergillosis had classified the disease into two types: the "superficial" involving the bronchi or trachea; and the "deep" or "ulcerative" form, involving the parenchyma of the lung. Probably better terms would be bronchial and pulmonary forms. This discussion will be confined to the latter type. Certainly, there is a great deal of overlapping between the two forms.

Patients who have pulmonary aspergillosis may or may not have symptoms when first seen by the physician. The patient under discussion and the case of Yesner and Hurwitz[11] and Vellios and his co-workers[10] had no symptoms relating to their pulmonary disease. If symptoms are present they often resemble those of chronic pulmonary tuberculosis. Hertzoz,[5] Hockberg,[7] Gerstl,[4] Friedman,[3] and Hughes[6] and their associates report patients who had one or more of the following symptoms: cough, fever, chest pain, and hemoptysis. In Hockberg's case, hemoptysis was a major problem requiring blood transfusions. The duration of symptoms in the cases reported varied from weeks to years.

Roentgenographic findings in pulmonary aspergillosis vary tremendously. In the cases of pulmonary aspergillosis reported, there was an increase in density in one or both lungs which was diffuse or localized. Van Ordstrand's[9] patient had bilateral infiltrations extending out from each hilum—a pattern which some authors have called the "sun burst" effect. This patient and those of Gerstl, Hockberg, Hughes, and Vellios had radiographic evidence of a cavity or questionable cavity present in the upper lobe of a lung.

The series reviewed and collected by Levin[8] includes 27 cases of pulmonary intracavitary "fungus ball" demonstrated radiologically. Of these, 22 were identified by culture as *Aspergillus fumigatus* and 5 as *Candida albicans*. The author described very clearly the mechanism of these roentgenologic characteristics. The fungus multiplies within the cyst, or cavity, producing an ovoid mass, and the surrounding varying densities of wall of cavity and lung parenchyma produce the pattern of a thin-walled cavity containing a central mass, often with a halo of air. This fungus ball was seen to change position in several instances. Vellios reports a similar case in which an intracavitary "fungus ball" was present. In the case reported here, the fungus mass in the cavities was interpreted as a fluid level. However, gross examination of the specimen revealed no fluid and the central mass was composed of necrotic debris and branching hyphae. Fluid levels to date have not been reported in this process.

Grossly, pulmonary aspergillosis may produce grayish-white nodules in both lungs. However, in many of the cases reported, the disease was confined to one lung or lobe, in which there was a grayish-white area of consolidation. There is often necrosis of tissue and cavity formation. The lobe of the lung in this case contained one large cavity and several smaller ones. All the patients on whom surgical resection of lung has been performed have had a cavity in the upper lobe or, much less commonly, apices of the lower lobes.

Microscopically, Aspergillus may produce a nonspecific inflammatory reaction or a chronic granulomatous response, the latter being defined as the proliferation of reticulo-endothelial cells or macrophages in which granules or nodules are formed. In this case there was a granulomatous reaction with multinucleated cells present. From the experimental work of Cooper,[2] it may be inferred that the fungus first produces a nonspecific inflammatory reaction which later may become granulomatous if enough time elapses. In Cooper's experiments with rabbits, 6 days were required for the lesions to become granulomatous.

The fungus is seen in the tissue as branching septate hyphae. In our patient, colonies of the fungus were found in the cavity as well as hyphae in the wall of the cavity, with a cellular reaction around them. This latter finding, we feel, eliminates the possibility that these organisms might have been a contaminant. To definitely establish the diagnosis of aspergillosis, the fungus must be cultured from the lesion and a reaction to the hyphae must be seen in the tissue. As pointed out by Hughes, this fungus in the tissue has to be distinguished from Mucor and Candida.

Treatment of this disease in the lung would seem to depend on whether the disease is localized to a lobe or an entire lung, or whether both lungs are involved. Van Ordstrand's patient, in which there was bilateral pulmonary infiltration without cavity formation, was treated with iodine with apparently good results. In this case and those of Hoekberg, Gerstl, Hertzoz, Yesner, Hughes, Friedman, and Vellios, removal of a localized lesion by lobectomy or lobectomy with segmental resection proved a very satisfactory method of treatment. Conant states that iodine therapy should be given after the surgical procedure. However, before conclusions can be drawn concerning treatment, more experience will be necessary.

SUMMARY

The clinical, roentgenographic, and pathologic findings and treatment of a case of primary pulmonary aspergillosis have been reported and discussed. This disease should be considered in any patient with localized or diffuse pulmonary lesions with or without symptoms.

This case is the eighth case of localized primary pulmonary aspergillosis treated by lobectomy reported in the United States to date.

We wish to thank the Department of Bacteriology, Bowman Gray School of Medicine, for its cooperation and Dr. Kenneth B. Raper, Department of Bacteriology, College of Agriculture, University of Wisconsin for identifying the fungus. The photographs and photomicrographs were prepared by Messrs. Ben Morton and Thomas Webster.

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FENESTRATED CARDIOVASCULAR CLAMPS

CHARLES P. BAILEY, M.D.,* AND BENJAMIN G. MUSSER, M.D.**
PHILADELPHIA, PA.

INTRODUCTION

ONE of the most obvious and pressing needs in the performance of major cardiovascular surgery is for a type of vascular clamp which will not cut through, crush, or perforate the delicate structures involved. The clamp must hold securely without danger of slippage. If, for certain conditions, it also can provide for suturing of approximated vascular walls without the necessity for prior division of their substance, a great additional advantage is obtained. Thus, each end of a patent ductus arteriosus might be occluded by separate mattress suture lines before interruption of its continuity. Likewise, the base of a ventricular aneurysm might be sutured before amputating the sac.

DESCRIPTION OF CLAMPS

The first of these clamps to be devised was the fenestrated aortic clamp (Fig. 1, *A*). This clamp was patterned after the large Satinsky aortic clamp. With the Pilling† Atraugrip surface of closure, it provides secure holding ability without risk of crushing or perforating delicate vascular structures. It is used for repair of the arterial incision employed for supravalvular approach for aortic commissurotomy. The clamps are designed to be applied so as to occlude the lips of an aortic incision, without compromising blood flow through the residual lumen. After completing the definitive surgery, the everted aortic lips are sutured by passing a double row of continuous No. 4-0 silk mattress sutures through the fenestrations in the blades of the clamp. Thus, a secure hemostatic closure may be effected even though only a narrow margin of the aortic wall may remain. An additional advantage is afforded in that the clamp regulates the depth of tissue through which each needle passes, assuring an even closure and minimizing the possibility of aortic tearing. The initial application of this clamp was such a success that an entire series of fenestrated clamps has been designed for other uses in cardiovascular surgery.

A fenestrated aortic clamp, in two sizes, was devised to facilitate plication of the aortic valve annulus (Fig. 1, *B1* and *B2*). This technique is effective in the treatment of aortic insufficiency when the valvular pathology consists basically of a relative or actual dilatation of the annulus. The beak of this

This work was done during the tenure of a National Heart Institute Traineeship in Thoracic Surgery at Hahnemann Medical College and Hospital.

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**Chief of Department of Cardiovascular Surgery, Harrisburg Hospital, Harrisburg, Pa.

†George P. Pilling & Son Co., Philadelphia, Pa.

clamp is straight, but scalloped, allowing it to be applied to include a portion of the annulus at its tip. While the instrument conceivably might be applied in a closed type of operation, it is intended for use in the open technique, a cardiopulmonary bypass being employed during the actual surgical procedure. The right atrium is mobilized to expose the right posterolateral sinus of Valsalva. This fenestrated aortic clamp may be applied so as to plicate the portion of the annulus which subtends the posterior, noncoronary bearing cusp. This creates a functionally bicuspid valve. The insufficiency is obliterated due to the relatively greater reduction in the cross-sectional area of the aortic orifice than in the circumference of the annulus (⅔ versus ⅓). The two remaining cusps become competent by reason of the reduction in the remaining valve area. At the conclusion of the annular plication, that portion of the sinus of Valsalva and of the ascending aorta which is grasped by the blade of the diagonally reapplied clamp is sutured through the fenestrations in a continuous mattress fashion. This extension or elongation of the zone of narrowing reduces the diameter of the aorta for some distance above the valve and relieves to some degree the tension which otherwise necessarily would be borne entirely by the sutures in the annulus itself.

Fenestrated ductus arteriosus clamps, in two sizes, have been designed to permit suture closure of the ends of this structure prior to actual division (Fig. 1, *C*). The gripping surface of these clamps is made narrower to facilitate their use in children and in patients with a short ductus arteriosus. When division has been decided upon, the ductal lumen is obliterated by sutures placed through each of two slotted clamps. The ductus then may be divided between the clamps without the risk of possible slippage and severe hemorrhage. The clamps are removed separately from the ductal ends, permitting methodical oversewing and additional sutures should stitch hole bleeding occur.

A similar type of clamp has been developed for use in coarctation of the aorta (Fig. 1, *D*). The jaws of these clamps are longer and of heavier construction than the ductus clamps. The double line of compression and the intervening slots of these clamps provide a more certain grip upon the ends of the divided aorta, do not crush or perforate the tissues, and practically preclude the possibility of slippage.

The aortic stenosis clamp has been modified as suggested by Morse for use in resection of aneurysms of the left ventricle (Fig. 1, *E*). This ventricular clamp has long angulated teeth attached to the inferior margin of the gripping surface (limb below the fenestration). The clamp is applied to the aneurysm so that when closed it will approximate the cicatrix at the base of the sac. The teeth prevent slippage during the next step. The fundus of the aneurysmal sac is incised widely with the clamp closed only partially (but with teeth securely engaged). Any contained loose clots are flushed out of the sac by the force of the next ventricular contraction. Then, the clamp is closed completely and the aneurysmal portion of the scar is excised. Heavy nonabsorbable mattress sutures are used for the repair, being placed through the fenestration in the clamp. The tissue about the base of the sac is sufficiently fibrous

to hold sutures easily. The clamp then may be removed and the suture line reinforced with a continuous running suture, assuring a double row for adequate hemostasis.

The pulmonary artery clamp was constructed with angulated jaws which close in a duckbill fashion (Fig. 1, *F*). This slotted clamp was devised for use

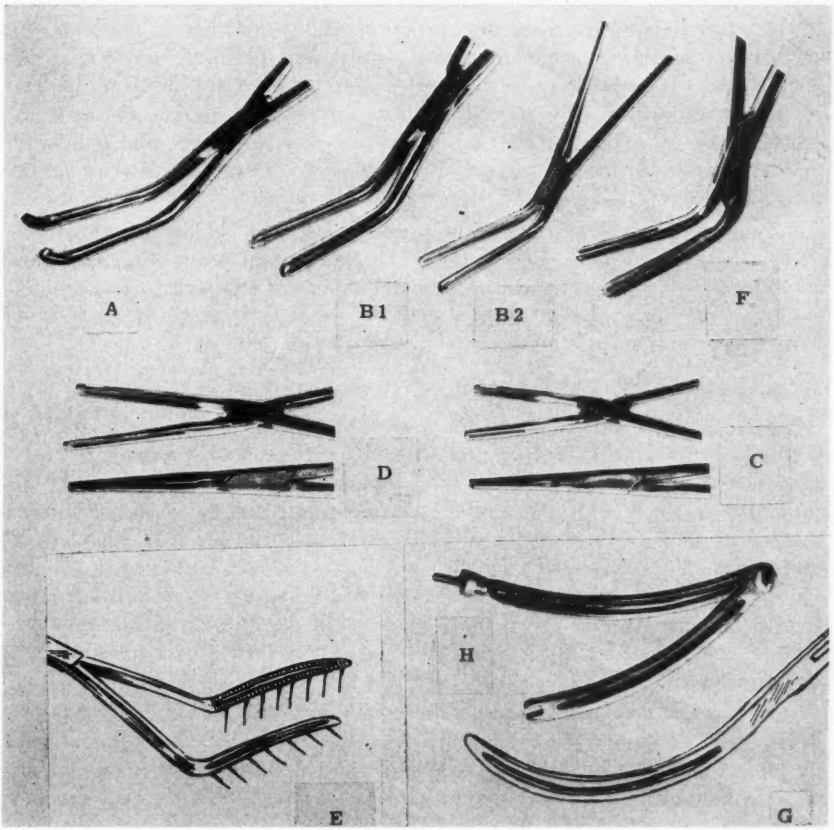

Fig. 1—*A*, Aortic stenosis clamp, fenestrated. This clamp is used in repair of the arterial incision used in aortic commissurotomy.

B1 and *B2*, Aortic insufficiency clamp, fenestrated. This clamp is used for plication of the base of the aorta in the correction of aortic insufficiency by cross fusion of the annulus.

C, Ductus arteriosus clamp, fenestrated. The jaws are flattened and thin. Before division of the ductus, each end is sutured through the fenestration. Then the ductus may be divided between the two clamps without risk of possible slippage and severe hemorrhage.

D, Coarctation clamp, fenestrated. The jaw of the clamp is longer and heavier than the ductus type. They provide a more certain grip upon the ends of the divided aorta.

E, Ventricular clamp, fenestrated. This clamp was modified by applying teeth to the lower edge of the jaw. This allows a firm grip on the myocardium while any intraluminal clot is flushed from between the jaws of the partially opened clamp by incising the fundus of the aneurysm.

F, Pulmonary clamp, fenestrated. This clamp is designed for clamping, suturing, and surgical interruption of an aortic septal defect.

G, Curved clamp, fenestrated. This clamp is designed for exclusion of a portion of the aorta or of the atrial wall.

H, Modified Cowley aneurysm clamp, fenestrated. This clamp is designed for cross-clamping of the base of an aortic aneurysm.

in aortic septal defects (aorticopulmonary fistulas). Two parallel slotted clamps are applied across the communication. Mattress sutures are passed through the fenestrations to secure intimal approximation. Both ends of the fistulous passage are thus sutured before the communication is divided. After division, the clamps are removed and the suture line is reinforced with a continuous row of No. 5-0 silk applied to the cut margins.

A curved clamp has been designed to exclude a portion of the wall of a vascular compartment such as the aorta, a great vein, or an atrium (Fig. 1, *G*). Such a clamp is useful in excision of arterial aneurysms, in the closure of tears in the atrial wall, and in partial resection of the left atrium for extensive bronchogenic carcinomas. The Atraugrip jaws assure a firm even grip while the defect is closed by placement of continuous or interrupted mattress sutures through the fenstrations.

Fenestration and an Atraugrip surface have been added to improve the Cowley aneurysm clamp (Fig. 1, *H*). The fenestration again offers the added advantage of ease of suturing with minimal chance of slippage. Firm approximation of the lips of the aneurysmal neck or base is maintained by a nut which is used to approximate the jaws of the clamp.

SUMMARY AND CONCLUSIONS

The incidence of slippage and possible laceration of the aortic wall has been reduced markedly during transarterial aortic commissurotomy by either the closed or open technique since the adoption of the fenestrated clamp. The jaws are designed with the Pilling Atraugrip surface for even nonslipping fixation of the structures grasped. This Atraugrip surface is present on both margins of the fenestration. In effect, the holding ability is that of two similar parallel clamps of the nonfenestrated type with the added significant advantage that slight extrusion of the tissue surface through the intervening slots provides. The wide gripping surface of the clamp offers secure hemostasis with less pressure upon the blood vessel wall.

A series of fenestrated clamps for use in cardiovascular surgery has been developed. These clamps offer the advantage of a double Atraugrip surface with an intervening slotlike fenestration and provide a convenient method of securing adequate hemostasis with minimum risk of tearing, crushing, or perforation of the tissues.

LUNG EXCLUSION CLAMP*

A New Instrument for Wedge Resections

Theodore R. Hudson, M.D.
Chicago, Ill.

A CLAMP has been devised which will be helpful in performing wedge resections for isolated pulmonary nodules and for lung biopsy. In the use of *two* curved clamps to exclude the wedge of lung to be removed, there is generally a certain amount of unavoidable awkwardness in coordinating the movements of the two clamps while laying the first line of sutures. Also, there is frequently a bleeder where the points of the two clamps meet but fail to secure the amputation line completely. While these difficulties are certainly not monumental, they are annoying and may be time-consuming. They are eliminated by this new instrument.

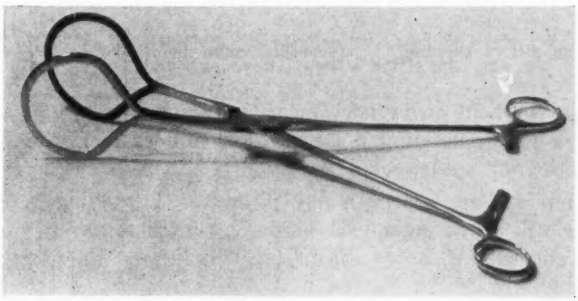

Fig. 1.—Lung exclusion clamp.

TECHNIQUE

The lung exclusion clamp is applied to the wedge of lung to be removed and the lock set down. The clamp has a soft action and will not mangle pulmonary tissue. A running mattress suture is taken below the clamp and close to it and tied at each end, leaving a 2-inch tail for traction at each knot. The wedge of lung is excised inside the clamp and close to it, and the instrument removed.

From the Surgical Department of Northwestern University Medical School and the Surgical Service, Chicago Wesley Memorial Hospital.
Received for publication July 15, 1957.
*Made by George P. Pilling & Son Company, Philadelphia, Pa.

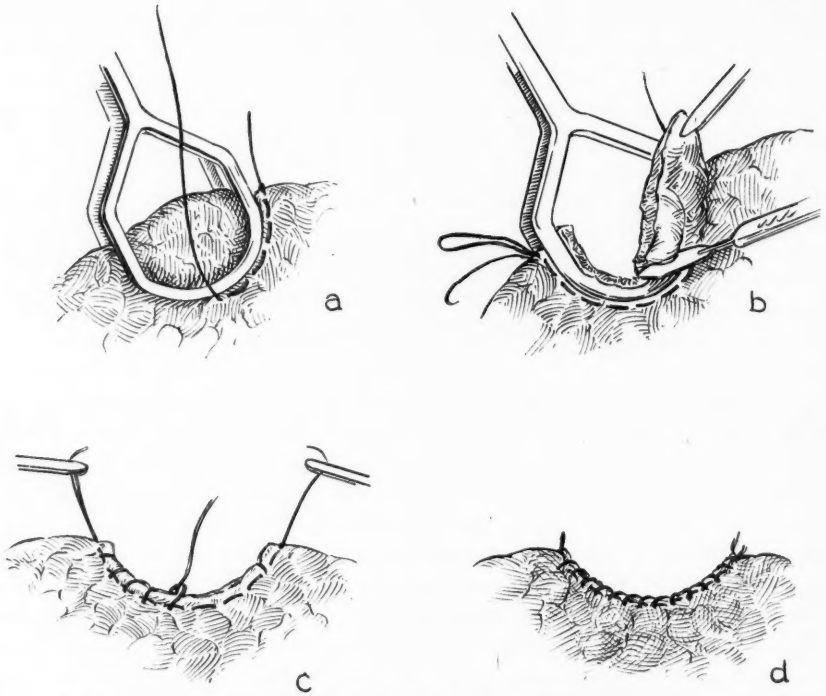

Fig. 2.—Technique for use. It is important to place the running mattress suture below the clamp before excising the specimen because the action of the instrument is so soft it will not hold the lung if the specimen is cut out first.

The lung may be held up by traction on the knot tails as the same suture is brought back to the starting point as a continuous lock-stitch, taken a bit deeper than the first suture line.

The clamp is 32 cm. in length and the opening in the jaws is 6.3 cm. across. This opening will accommodate the largest nodule one would care to resect by this method and will, of course, accept anything less, so that more than one size is not required.

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

THIRTY-EIGHTH ANNUAL MEETING
MAY 16, 17, AND 18, 1958
HOTEL STATLER, BOSTON, MASS.

Program

MEMORANDA FOR GUIDANCE OF SPEAKERS

1. In accordance with the By-Laws of the Association the papers which are read at the Meeting shall be given to the Reporter *immediately after presentation.* If these papers are not submitted promptly their publication may be delayed.
2. In publication it is customary to group discussions together on a series of papers. Any delay in the return of corrected discussions to the Editor means that publication of all papers on the subject will be held up. This is manifestly unfair to those who are conscientious in the prompt submission of their remarks for publication. Undue tardiness may mean that the discussion will not be published.
3. *Regular Program.*—Speakers (except in symposia) will be limited to 15 minutes for presentation.
4. *Thoracic Surgery Forum.*—Speakers will be limted to 10 minutes for their presentations. Papers on the Thoracic Surgery Forum as submitted for publication will be limited to 3,000 words. At the discretion of the President and within the limits of the allotted time, one or more discussions per paper will be allowed following all formal presentations.
5. *Discussion of Papers.*—Discussers will be limited to 3 minutes. Only members of the Association and invited speakers will have the privilege of discussing papers.

MOTION PICTURE SESSION

Motion pictures will be shown on May 16, 17, and 18. Please consult official program for titles.

Friday Morning, May 16, 1958

8:30 A.M. Business Meeting.
Scientific Session: REGULAR PROGRAM

Eulogy: Evarts A. Graham, by Tom Burford.

1. **Further Studies in the Surgical Management of Carcinoma of the Lung.** Edward D. Churchill, Richard H. Sweet, J. Gordon Scannell, and Earle Wilkins (by invitation), Boston, Mass.
2. **Should We Insist on "Radical Pneumonectomy" as a Routine Operation for Carcinoma of the Lung?** Julian Johnson, Charles K. Kirby, and William S. Blakemore (by invitation), Philadelphia, Pa.
3. **Results in the Treatment of Bronchogenic Carcinoma—An Analysis of 1,008 Cases.** Sol Center (by invitation), Miami, Fla., and Thomas H. Burford, St. Louis, Mo.
4. **Coronary Artery Disease After 25 Years.** Claude S. Beck, Cleveland, Ohio.
5. **The Clinical Significance of Cor Pulmonale in the Reduction of Cardiopulmonary Reserve Following Extensive Pulmonary Resection.** William E. Adams, Robert W. Harrison (by invitation), Edwin T. Long (by invitation), and Benjamin Burrows (by invitation), Chicago, Ill.

6. **Effect of Severe Unilateral Hypoxia on the Partition of Pulmonary Blood Flow in Man.** Aaron Himmelstein, P. Harris (by invitation), H. W. Fritts, Jr. (by invitation), and Andre Cournand, New York, N. Y.

Friday Afternoon, May 16, 1958

2:00 P.M. Scientific Session: REGULAR PROGRAM

Address by the President, Brian Blades, Washington, D. C.

7. **Surgical Treatment of "Atypical" Patent Ductus Arteriosus.** William P. Young (by invitation), George G. Rowe (by invitation), Anthony R. Curreri, and Joseph W. Gale, Madison, Wis.
8. **Intrathoracic Aneurysms of the Aorta—Analysis of 160 Cases Treated by Resection.** Michael E. DeBakey, Denton A. Cooley, E. Stanley Crawford (by invitation), and George C. Morris, Jr. (by invitation), Houston, Texas.
9. **Experiences With the Davila-Glover Purse-String in the Correction of Mitral Insufficiency: A Critical Appraisal.** Edward M. Kent, William B. Ford, John F. Neville, Jr. (by invitation), and Don L. Fisher (by invitation), Pittsburgh, Pa.
10. **Technical Considerations in Decortication for the Pleural Complications of Pulmonary Tuberculosis.** Paul C. Samson, Duane L. Merrill (by invitation), David J. Dugan, Oakland, Calif., E. J. Shabart (by invitation), Livermore, Calif., Louis Barber (by invitation), Stockton, Calif., and James Yee (by invitation), Oakland, Calif.
11. **Achalasia of the Esophagus—Further Thoughts on Surgical Management.** William M. Tuttle, Detroit, Mich., and Robert T. Crowley (by invitation), Williamson, W. Va.

Saturday Morning, May 17, 1958

8:30 A.M. Scientific Session: THORACIC SURGERY FORUM.

12. **The Simplified Stationary Screen Pump-Oxygenator.** Jerome Harold Kay (by invitation), and Robert M. Anderson (by invitation), Los Angeles, Calif.
13. **Comparison of Relative Merits of Occlusive and Nonocclusive Pumps for Open Heart Surgery.** Paul C. Hodges (by invitation), C. Walton Lillehei, Richard Cardozo (by invitation), Andre Thevenet (by invitation), Minneapolis, Minn.
14. **Cardiac Bypass Without Artificial Oxygenator.** W. T. Mustard (by invitation), W. Sapirstein (by invitation), and Denise Pav (by invitation). Sponsored by F. G. Kergin, Toronto, Canada.
15. **Monitor and Control of Blood Oxygen Tensions and pH During Total Body Perfusion.** Leland C. Clark, Jr. (by invitation), Samuel Kaplan (by invitation), Edward C. Matthews (by invitation), F. Kathryn Edwards (by invitation), and James A. Helmsworth, Cincinnati, Ohio.
16. **Experimental and Clinical Studies of Controlled Hypothermia Rapidly Produced and Corrected by a Blood Heat Exchanger During Extracorporeal Circulation.** Ivan W. Brown, Jr. (by invitation), Wirt W. Smith (by invitation), W. Glenn Young (by invitation), and W. C. Sealy, Durham, N. C.
17. **Cerebral Blood Flow and Brain Volume Changes in Extracorporeal Circulation.** Max M. Halley (by invitation), Keith Reemtsma (by invitation), Manuel Bresler (by invitation), and Oscar Creech, Jr., New Orleans, La.
18. **Clotting Deviations in Man During Cardiac Bypass—Fibrinolysis and Circulating Anticoagulant.** Kurt von Kaulla (by invitation), and Henry Swan, Denver, Colo.

19. **Elective Cardiac Arrest: The Relationship of Elevated Intracardiac Pressures to Subsequent Myocardial Function and Pathologic Pulmonary Changes.** John Ross, Jr. (by invitation), Joseph W. Gilbert, Jr. (by invitation), Edward H. Sharp (by invitation), and Andrew G. Morrow, Bethesda, Md.
20. **Lung Lymph in Experimental Pulmonary Edema.** A. Robert Cordell (by invitation), Winston-Salem, N. C., Richard A. Bahn (by invitation), Buffalo, N. Y., James C. Stephens (by invitation), Buffalo, N. Y., and H. H. Bradshaw, Winston-Salem, N. C.
21. **The Effect of Position on Pulmonary Ventilation.** Thomas F. Nealon, Jr. (by invitation), and John H. Gibbon, Jr., Philadelphia, Pa.
22. **Aortic Homograft Replacement of the Main Pulmonary Artery.** George Robinson (by invitation), Philip Glotzer (by invitation), Marvin Gilbert (by invitation), and Elliott S. Hurwitt, New York, N. Y.
23. **Experimental Results With a Prosthetic Aortic Valve.** Benson B. Roe, John W. Owsley (by invitation), and Peter C. Boudoures (by invitation), San Francisco, Calif.
24. **Post-mortem Perfusion Studies in the Evaluation of Techniques of Aortic Valvulotomy.** W. Gerald Austen (by invitation), Robert S. Shaw (by invitation), W. M. Thurlbeck (by invitation), and J. Gordon Scannell, Boston, Mass.
25. **Intercoronary Collaterals in Normal Hearts.** Sven Bellman (by invitation), and Howard A. Frank, Boston, Mass.
26. **Changes in Pulmonary Artery Pressure During Cardiopulmonary Bypass: An Experimental Study.** James B. Littlefield (by invitation), J. Francis Dammann, Jr., Phyllis R. Ingram (by invitation), and William H. Muller, Jr., Charlottesville, Va.

Saturday Afternoon, May 17, 1958

2:00 P.M. Executive Session. (Limited to Active and Senior Members.)

3:30 P.M. Scientific Session: REGULAR PROGRAM

27. **Intrathoracic Pheochromocytomas.** Herbert C. Maier, and George H. Humphreys, New York, N. Y.
28. **Management of Staphylococcic Tension Pneumatoceles by Intracavitary Suction Tube Drainage.** Elton Watkins, Jr., and Alexander C. Hering (by invitation), Boston, Mass.
29. **Topography of the Human Coronary Arteries Considered in Relation to Cardiac Surgery.** Thomas N. James (by invitation), and George E. Burch (by invitation). Sponsored by Alton Ochsner, New Orleans, La.

7:00 P.M. BANQUET AND DANCING, Hotel Statler.

Attendance limited to Members of the Association and their ladies, invited speakers and their ladies.
Dinner dress preferred.

Sunday Morning, May 18, 1958

8:30 A.M. Scientific Session: REGULAR PROGRAM

30. **Open Operation for Mitral Insufficiency.** Donald B. Effler, Laurence K. Groves, William V. Martinez (by invitation), and Willem J. Kolff (by invitation), Cleveland, Ohio.
31. **Direct Vision Correction of Mitral Regurgitation.** Earle B. Kay, and Cid Nogueira (by invitation), Cleveland, Ohio.
32. **Satisfactory Surgical Correction of Pectus Excavatum Deformity in Childhood—A Limited Opportunity.** Kenneth J. Welch (by invitation), Boston, Mass.

33. **Pectus Excavatum: An Appraisal of Surgical Treatment.** Paul C. Adkins (by invitation), and Owen Gwathmey, Washington, D. C.
34. **Hypoventilation, Hypoxia, and Acidosis Occurring in the Acute Postoperative Period.** R. Maurice Hood (by invitation), and Arthur C. Beall, Jr. (by invitation), Oakland, Calif. Sponsored by Frank Gerbode, San Francisco, Calif.
35. **Clinical and Hemodynamic Evaluation of the Surgical Correction of Aortic Stenosis.** Dwight E. Harken, Harrison Black, Warren J. Taylor (by invitation), Wendell B. Thrower (by invitation), Harry S. Soroff (by invitation), Steven Lunzer (by invitation), and Roy H. Clauss (by invitation), Boston, Mass.
36. **The Surgical Treatment of Anomalous Pulmonary Veins.** Henry T. Bahnson, and Frank C. Spencer (by invitation), Baltimore, Md.

Sunday Afternoon, May 18, 1958

2:00 P.M. Scientific Session: REGULAR PROGRAM

37. **Pulmonary Resection in the Treatment of Tuberculosis—Experience With 1,700 Cases.** Raymond J. Barrett (by invitation), Richard Jankoska (by invitation), J. Claude Day, Paul V. O'Rourke, and E. J. O'Brien, Detroit, Mich.
38. **Pulmonary Infarction Complicating Segmental Resection.** John M. Salyer, and Harold N. Harrison (by invitation), Denver, Colo.
39. **Creation of a Temporary Artificial Ductus in the Surgical Correction of Ventricular Septal Defects Associated With Severe Pulmonary Hypertension: A Two-Stage Operation.** Howard D. Sirak (by invitation), and Don M. Hosier (by invitation). Sponsored by H. William Clatworthy, Jr., Columbus, Ohio.
40. **Corrective Surgery in the Presence of Far-Advanced Pulmonary Hypertension.** C. Walton Lillehei, Donald J. Ferguson (by invitation), and Richard L. Varco, Minneapolis, Minn.
41. **Surgical Treatment of the Tetralogy of Fallot by Open Intracardiac Repair.** John W. Kirklin, F. Henry Ellis, Jr., and Dwight C. McGoon (by invitation), Rochester, Minn.
42. **Atrial Septal Defect, Secundum: Observations on One Hundred Patients Treated by Open Operation.** Henry Swan, Denver, Colo., D. Hywel Davies (by invitation), and S. Gilbert Blount, Jr. (by invitation), Denver, Colo.